The Oxford Medicine

BY VARIOUS AUTHORS

VOLUME II

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CHAPTER I

INFECTIONS OF THE UPPER AIR PASSAGES AND THEIR RELATION TO GENERAL SYSTEMIC DISORDERS

By S. J. CROWE and JOHN W. BAYLOR

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INFECTIONS OF THE UPPER AIR PASSAGES

The recent work on the bacterial flora of the upper air passages in health and disease and the data on the etiology of the "common cold" are the natural starting points for any discussion of upper respiratory tract infections. Kneeland[1] in 1930 took cultures from the nasal passages and throat of thirty infants immediately after birth and obtained no growth in 85 per cent; even on the second day the cultures were sterile in 40 per cent. Later the staphylococcus, various types of streptococcus, the pneumococcus and the influenza bacillus appear. The beta hæmolytic streptococcus is by far the most common organism found in infections of the ear, the accessory nasal sinuses and the tonsils. Bloomfield finds that acute tonsillitis is invariably caused by this organism. Bourn, Carpenter and McComb[3] find the beta hæmolytic streptococcus in 9.3 per cent of 190 cultures from healthy individuals, in 9.5 per cent of 585 cultures from patients with an acute coryza or the "common cold," and in 45.8 per cent from patients with an acute tonsillitis. During the epidemics of streptococcal disease in army camps in 1917–1919 almost every man, both the sick and the well, harboured this organism in his throat. Under these conditions the beta hæmolytic streptococcus grows on the surface of the mucous membrane of the pharynx, but under ordinary conditions it is found only in the presence of an acute infection or in from 9 to 12 per cent of healthy persons who are "carriers." The Thomsons[4] conclude that the

pneumococcus streptococcus B influenzæ and M catarrhalis are the cause of the common cold but Kruse[4(a)] (1914), Foster[4(b)] (1917), Dochez[5] (1930), Long[6] (1931) and others have shown that it is due to a filterable virus

As a rule, mild cases of respiratory catarrh are called "colds", and the more severe cases with fever are called influenza There is considerable evidence that both are caused by a filterable virus During the pandemic of 1918–1919 attempts were made to demonstrate a filterable virus Both human volunteers and monkeys were inoculated with filtrates of sputum and blood from patients ill with influenza All inoculated volunteers except those who had just recovered from an attack developed symptoms of this disease within 48 hours At the same time attempts to transmit influenza to healthy volunteers by means of pure cultures of Pfeiffer's bacillus were uniformly negative Crowe and Thacker Neville[7] found the Pfeiffer's bacillus in 21 per cent of infected maxillary sinuses during non-epidemic years and in 26 per cent during the severe influenza epidemic of 1918–1919 They conclude that this organism is a secondary invader and not the cause of the disease known as influenza Bourn[8], in 193?, reports the results of a systematic study of the frequency of B influenzæ (Pfeiffer's bacillus) in Baltimore from October 1928 to September 1930 which includes the epidemic period of 1928–1929 B influenzæ was found as prevalent in one season as another it was present in ?6 8 per cent of 858 naso-pharyngeal cultures from patients ill with an acute upper respiratory tract infection and in 25 6 per cent of 1742 cultures from healthy persons It is noteworthy that the relative frequency of B influenzæ in ill patients with a leucopenia was the same as that found in patients with a leucocytosis

A bacteriological study of colds on an isolated tropical island (St John)[9], where scarlet fever and diphtheria are unknown, showed the basic naso pharyngeal flora similar to that in Labrador and in the temperate zone and the seasonal incidence of colds the same as in the temperate zone In a study of the "common cold in Spitzbergen Paul and Freese[10] state that the entire community is infected within three days after the arrival of the first boat of the summer They conclude that the infection is due to a filterable virus It is well known that explorers may remain perfectly well in the region of the north pole for two or three years where they are exposed to excessively cold weather and fatigue but always develop an upper respiratory tract infection as soon as they return to a community where colds are prevalent Long[11] and his associates in 1931 report transmission experiments from patients ill with influenza to anthropoid apes Three apes had fever prostration and leucopenia within 48 hours after intranasal inoculation with bacteria free filtrates of nasal washings from patients ill with influenza The inoculation of a fourth ape with a similar bacteria free filtrate which had been in the ice box for 1-3 days also produced after 7 hours a typical influenzal infection This

seems to prove conclusively that the disease we call influenza is due to a virus and not to any of the pyogenic organisms

As regards *treatment* everyone agrees that rest in bed is a wise precaution against complication The use of nasal douches and sprays probably is harmful since they may interfere with the activity of the cilia Doull Hardy Clark and Herman[1] in 1931, report their observations on the effect of ultra violet light treatments for the prevention of the common cold They employed two groups of students one group numbering 170 was irradiated at regular intervals and the dosage accurately measured 184 students were used as a control group Bacteriologic studies of the upper air passages were made on both groups and a daily record kept of the incidence and the local and general symptoms of respiratory infections The number of colds contracted by the two groups was so nearly equal that these observers conclude that ultra violet light exposures do not protect against the common cold

Vitamin A is often called the anti infective vitamin and is believed to be especially valuable in the prevention of bacterial invasion of mucous membranes Because of this alleged protective value substances containing this vitamin are recommended and sold as an effective means to prevent colds Shibley and Spies[13] in a carefully controlled experiment on 241 young adults reached the conclusion that vitamin A has no effect on the incidence or severity of the common cold Other observers have shown that it is of no value in pneumonia tuberculosis as a prophylactic measure for colds in infants and school children or to reduce the incidence of otitis media in scarlet fever

The public takes more medicine for colds than for the treatment of any other illness The Thomsons[4] in their exhaustive review of 2 000 papers on the common cold conclude that the use of drugs may be of some value but as a rule they fail to produce the desired effect Diehl[14] in 1933 concludes from his study of the treatment of colds carried out on a large volunteer group at the University of Minnesota that sodium bicarbonate acetylsalicylic acid and a combination of this latter drug with acetphenetidin-caffeine gave no better results than the lactose tablet used in his control group Only opium and certain alkaloid derived from it seem to be of value in the treatment of acute coryza They found that the combination of codeine 15 mg ($\frac{1}{4}$ gr) with papaverine 15 mg ($\frac{1}{4}$ gr) was followed by a prompt decrease or a complete disappearance of the nasal discharge and congestion in 161 or 75 per cent of the 216 individuals who were given this combination during the acute stage of a cold None of the various drugs used in this experiment were of any value in shortening the duration of subacute or chronic colds The dosage of this codeine papaverine combination varies with the weight of the patient 75 to 99 pounds 1 after breakfast at bedtime 100 to 1 9 pounds 1 after breakfast 3 at bedtime 130 to 169 pounds 1 after breakfast 1 after lunch

3 at bedtime 170 pounds and over 1 after each meal, and depending on the weight, 3 or 4 at bedtime

Since the evidence seems to indicate that the common cold is due to a virus rather than to bacteria it is difficult to see how either stock or autogenous vaccines could be of any value in the prevention of colds As a matter of fact however, both of these varieties of vaccine do seem to help some patients The subcutaneous injection of any protein may have the same effect Our present attitude is that if the dosage is carefully regulated, vaccines can do no harm and may lessen the frequency of colds, or at least the complications of colds

Infection of the Nose and the Accessory Nasal Sinuses

The mucous membrane lining the nasal cavities and the accessory nasal sinuses forms a continuous sheet, which is rich in blood vessels and mucus secreting glands It is covered with ciliated epithelium, and in addition to mucus it secretes a substance called lysozyme The layer of viscid mucus, the activity of the cilia and the inhibiting action of lysozyme are all factors in the protection against infection Linton[1] Proetz, Hilding[3], Lierle and Moore[4] Negus and others have studied the ciliary activity in experimental animals after the introduction of various drugs commonly used in clinical practice Due to the constantly moving layer of mucus it is impossible to sterilize the mucous membrane by the local application of any antiseptic Adrenalin even in the dilution of 1 to 5000 cocaine in any concentration greater than 2 5 per cent, silver nitrate, thymol eucalyptus and merthiolate all impair the activity of the cilia sometimes permanently On the other hand camphor and menthol of each 1 per cent in petrolatum ephedrine sulphate 3 per cent and the protein salts of silver are not harmful

The nasal passages are infected more frequently than any other locality in the body and with every infection the sinuses are probably involved The majority of these infections are due primarily to the 'common cold virus but pyogenic organisms play the chief role in the complications The symptoms of the common cold usually disappear within two or three weeks, if congestion, discharge and particularly headache general malaise and fever persist, a sinus infection should be suspected An acute sinus infection is the result of mechanical occlusion of the orifice by edema and thick mucous discharge, and the severity of the clinical symptoms depends on the degree of obstruction to drainage and the virulence of the organism If recognized during the acute stage all sinus infections can be cured by relatively simple local or operative measures which re-establish drainage if allowed to become chronic, however, the infection is often extremely difficult or impossible to cure

The pain of nasal sinus infection usually is unilateral worse in the early morning or early forenoon rather than in the afternoon or at night and limited to the area supplied by the trigeminal nerve When the frontal and ethmoidal sinuses are involved the pain is located in the forehead and around the eyes In maxillary or antrum infections the pain is more likely to be above the eye than directly over the infected sinus Sphenoidal sinus infection causes pain in the suboccipital region and across the bridge of the nose Pain is a symptom of sinus infection that cannot be ignored or controlled with drugs without endangering the life of the patient This is particularly true of acute infections of the frontal ethmoidal and sphenoidal sinuses Osteomyelitis of the skull frontal lobe abscess and meningitis are complications of frontal sinusitis while orbital cellulitis retro-bulbar neuritis and cavernous sinus thrombosis may result from an unrecognized or untreated ethmoidal or sphenoidal infection It is even more dangerous to relieve with drugs the pain of sinusitis without determining the cause than it is to give morphine for the pain of unrecognized acute appendicitis

The proper treatment of a patient with nasal sinus infection depends as much on a correct interpretation of the symptoms elicited in the history as it does on the objective findings of the examination for example a patient may have a sinus infection but his symptoms may be due in large part to migraine imbalance of the ocular muscles intracranial tumor or some systemic disorder The diagnosis of sinus infection must be made by correlating the symptoms elicited in the history with the findings on transillumination x ray and the local intra nasal examination Neither x ray nor transillumination findings alone justify the diagnosis of sinusitis without further study

Infections of the nasal sinuses in children are frequent and their recognition and treatment are of the greatest importance in pediatrics In almost every instance in which infection of the tonsils plays a part in systemic disease and particularly in acute renal disorders the condition of the sinuses must be checked repeatedly It is comparatively easy to clear up an infection in the tonsils or naso-pharynx by local treatment or a single operation an infection in the accessory nasal sinuses is quite a different matter The internist and pediatrician must realize that in the treatment of nasal sinus disease the infected area cannot be excised as the tonsil and it is a much better policy to do as little as possible and await results even if a second or a third operation is necessary rather than risk doing more than is necessary This applies particularly to the operative treatment of sinusitis in children The results of sinus work in selected cases certainly justify the operations that have been done but the pediatrician should first exhaust all of his therapeutic resources before an operative attack is made on the sinuses

The first step in the surgical treatment is to remove the cause which may

or infected teeth infected tonsils adenoids or the lymphoid tissue at the base of the tongue or obstructive lesions in the nose Allergic conditions must be controlled Proper food habits and exercise are important In the presence of a serious complication of acute sinus infection any operative measure is justifiable but in not more than one of a hundred children with chronic nasal sinus disease and systemic symptoms is it necessary to open the ethmoidal labyrinth When children have recurring colds and attacks of sinusitis, it is advisable for them to spend a part of each year in a climate where respiratory infections are less frequent particularly if they have an inherited tendency to hay fever or asthma Frequently however the advantages of the climate are counteracted by the sinus and ear infections acquired in swimming pools A laryngologist in Florida writes We have fully as many cases of sinusitis in our warm sunny Florida as there are in the North [6]

It is difficult to make a satisfactory examination of the nasal passages in some children without general anæsthesia The x ray examination as a diagnostic procedure is not conclusive or satisfactory unless supplemented by an examination with the nasal speculum the nasopharyngoscope, puncture and irrigation of the maxillary sinuses if indicated and a bacteriological and cytological study of any discharge for the presence of abnormal numbers of pathogenic organisms pus cells or eosinophiles

Infection may not be the cause but it must be searched for and eradicated in patients with the following conditions 1) bronchial asthma and all allergic conditions, 2) nephritis and nephrosis particularly acute glomerular nephritis 3) infections of the eustachian tube the middle ear the mastoid and its complications 4) orbital and ocular infections 5) headache or neuralgic pains in the head

The more prominent respiratory symptoms of asthma in children may disappear spontaneously To a less extent the same is true in adults but rarely, if ever do all of the allergic manifestations of this disease disappear It is difficult, therefore to evaluate any one therapeutic measure Asthmatic paroxysms must be regarded as a symptomatic expression of a constitutional disturbance, and every effort should be made to discover and correct all abnormalities that may contribute in any way to the basic disease The asthmatic or allergic tendency certainly is hereditary, and in an atopic child all respiratory infections however slight should be treated seriously Obstruction to breathing and a constant flow of infected discharge in the pharynx and into the trachea especially when asleep are common manifestations of a chronic sinusitis It has been our experience that in patients with bronchial asthma the clinical symptoms are not improved unless the obstruction to breathing has been relieved and the discharge has been stopped

This may require radical surgical operations Heatly and Crowe[7] in

1923 reported the results of the operative treatment of sinus infection in 6 patients with asthma While in an occasional patient excellent results were obtained by the removal of nasal polypi in the vast majority of cases such simple procedures proved either very transient in their effect or utterly useless An example of another allergic condition which may be benefited by the operative removal of focal infections is the report by Fink and Gay[8] in 1934 of 170 cases of urticaria and angio neurotic edema Their patients were followed for a period of from two to ten years In 52 patients or 30 per cent of the entire group the urticaria permanently disappeared after the foci of infection were removed More than three fourths of the infections were in the teeth or upper air passages

The discussion of nephritis and nephrosis as a complication of tonsillar infection applies equally well to nasal sinus infections The sinuses and the tonsils are in such close proximity that an infection of one usually spreads to the other The postnasal drainage of a chronic sinusitis infects the tonsils and lymph adenoid tissue in the nasopharynx and at the base of the tongue while coughing sneezing and violently blowing the nose are the common methods by which chronic tonsillar or chronic pharyngeal infection is implanted in the nasal sinuses and particularly in the ethmoidal cells The important thing to remember is that in more than three fourths of the patients with acute glomerular nephritis the infecting organism is the streptococcus and the focus of infection is located in the upper air passages Nephrosis is believed by some to be a degenerative disease but reports indicate that removal of infection is of distinct benefit in some cases In both conditions therefore a careful search must be made for infection The sharp differentiation of pharyngeal and nasal sinus infection is artificial in the presence of renal joint and other systemic disorders they should be regarded as one and every means at our disposal employed to recognize and eliminate infection in this region

The mastoid cells middle ear and eustachian tube are lined with mucous membrane which is continuous with that of the nose nasopharynx and pharynx Considering the frequency with which nasal mucous membrane is infected in the epidemic diseases of childhood and adult life it is remarkable that the ear is not involved more often Campbell[9] found objective evidences of nasal sinus infection in more than 90 per cent of 150 children with otitis media About 73 per cent of these children were less than two years of age In Fowler's[10] group of 100 children roentgen examination indicated that the sinuses were or had been infected in 86 per cent He was studying the relation of infection to impaired hearing There was a history of discharge or pain in the ear in 78 per cent Hoople and Cave[11] took x rays during the first week of scarlet fever and during convalescence and found the nasal sinuses involved in

be infected teeth infected tonsils adenoids or the lymphoid tissue at the base of the tongue or obstructive lesions in the nose Allergic conditions must be controlled Proper food habits and exercise are important In the presence of a serious complication of acute sinus infection any operative measure is justifiable but in not more than one of a hundred children with chronic nasal sinus disease and systemic symptoms is it necessary to open the ethmoidal labyrinth When children have recurring colds and attacks of sinusitis, it is advisable for them to spend a part of each year in a climate where respiratory infections are less frequent particularly if they have an inherited tendency to hay fever or asthma Frequently however the advantages of the climate are counteracted by the sinus and ear infections acquired in swimming pools A laryngologist in Florida writes We have fully as many cases of sinusitis in our warm, sunny Florida as there are in the North [6]

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that multiple sclerosis is the most common cause of this disease It is well known that developmental anomalies may leave the optic nerve in close proximity to the mucous membrane of the sinuses The impaired vision in retro-bulbar neuritis comes on suddenly and if it does not improve during the first three or four weeks a secondary atrophy of the nerve develops When the symptoms of retro bulbar neuritis appear in a patient who has a definite sinus infection it is generally agreed that everything possible should be done to improve drainage and that it should be done promptly and thoroughly The controversy is about the treatment of patients with retro-bulbar neuritis who have none of the usual signs and symptoms of ethmoidal or sphenoidal sinus infection It is true that enlargement of the blind spot and subjective dimness of vision are often the first evidences of multiple sclerosis that remissions are common in this disease and that some of the patients whose sinuses are opened as a therapeutic measure ultimately develop other symptoms of multiple sclerosis but this does not justify withholding the operation in doubtful case A positive diagnosis of multiple sclerosis cannot be made when impaired vision is the only symptom Many cases have been reported in which the vision promptly and permanently improved after apparently healthy posterior ethmoidal and sphenoidal sinuses were opened and no further symptoms of multiple sclerosis ever developed The operation is simple and devoid of danger and we feel that in all such doubtful cases the patient should have the chance of saving his vision that a sinus operation may offer If in these cases in which the etiology is doubtful the impaired vision is definitely ascribed to multiple sclerosis then there is nothing to do but hope for a spontaneous remission and wait and watch for other symptoms to confirm the diagnosis Due to the development of optic atrophy a delayed sinus operation is of no value

Infection of the Tonsils

A study of the histologic structure of the palatine tonsil offers an explanation for the fact that *it is one of the most common locations in the body for a chronic focus of infection* The crypts *ramify throughout the tonsils and are lined with squamous epithelium* The crypt *epithelium contains no mucous* glands to aid in clearing the crypts of debris or infection The epithelium lining the crypts contains a rich network of blood vessels differing in this respect from the epithelium covering the surface of the tonsil or the surrounding mucosa The microscopic study of several thousand diseased tonsils removed at operation and of a few normal tonsils removed at autopsy indicates that tonsillar infection always begins in a crypt destroys localized areas of the lining epithelium in mild infections and extensive areas in the more virulent infec

91 per cent of 383 cases In 33 patients a mastoid operation was necessary and in every case there was roentgenographic evidence of sinusitis as a rule the sinus and mastoid infections were on the same side

It is evident that infection of the ear frequently is associated with an infection of the accessory nasal sinuses The sinuses should therefore, be examined in all patients with otitis media or mastoiditis If the maxillary sinuses are infected they should be irrigated The other sinuses are best treated by measures that aid drainage The recognition and treatment of the nasal infection may shorten the duration of the otitis and possibly prevent some of the serious complications of mastoiditis

The development of the ethmoidal and sphenoidal sinuses is so irregular and varied that in some individuals the mucous membrane lining the sinus is in direct contact with the orbital contents or the sheath of the optic nerve These dehiscences in the bone probably explain why *some patients with an* acute sinusitis have orbital cellulitis and others escape any complications of this character Such developmental abnormalities may be seen in the anatomical dissections of Schaeffer in Philadelphia and the Onodi collection in the *Royal College of Surgeons in London*

The eye is affected by nasal sinusitis in three ways 1) by direct extension to the orbit from an infected ethmoidal or sphenoidal sinus 2) by direct extension to the conjunctiva through the lachrymal duct and 3) by the absorption of toxins

Preceding a surgical operation of any kind on the eye the sinuses should be examined A post-operative eye infection may result in a permanent loss of vision Chronic dacryocystitis is due to a stricture of the naso lachrymal duct and the cause of the primary stenosis is inflammation of the nasal mucous membrane Cellulitis of the orbit and retro-bulbar abscess are both serious conditions If the cellulitis is secondary to ethmoidal infection it may go on to abscess formation unless adequate intranasal drainage is established A retro-bulbar abscess often results in cavernous sinus thrombosis or meningitis and when secondary to sinus disease is best located and drained through an external incision Inflammation of the uveal tract (iris ciliary body and choroid) is one of the most serious and complex of all eye diseases The conditions giving rise to uveal tract inflammation fall into two groups 1) systemic disease — syphilis tuberculosis acute infectious diseases 2) foci of infection — tonsils teeth accessory nasal sinuses etc In addition to the local treatment and operations by the ophthalmologist the recognition and treatment of associated nasal sinus infection is an important part of the therapy

Opinions differ as to the importance of nasal sinus infection in the etiology and treatment of retro-bulbar neuritis It is thought by Gifford[1] and others

that multiple sclerosis is the most common cause of this disease It is well known that developmental anomalies may leave the optic nerve in close proximity to the mucous membrane of the sinuses The impaired vision in retrobulbar neuritis comes on suddenly and if it does not improve during the first three or four weeks a secondary atrophy of the nerve develops When the symptoms of retro bulbar neuritis appear in a patient who has a definite sinus infection it is generally agreed that everything possible should be done to improve drainage and that it should be done promptly and thoroughly The controversy is about the treatment of patients with retro-bulbar neuritis who have none of the usual signs and symptoms of ethmoidal or sphenoidal sinus infection It is true that enlargement of the blind spot and subjective dimness of vision are often the first evidences of multiple sclerosis that remissions are common in this disease and that some of the patients whose sinuses are opened as a therapeutic measure ultimately develop other symptoms of multiple sclerosis but this does not justify withholding the operation in doubtful case A positive diagnosis of multiple sclerosis cannot be made when impaired vision is the only symptom Many cases have been reported in which the vision promptly and permanently improved after apparently healthy posterior ethmoidal and sphenoidal sinuses were opened and no further symptoms of multiple sclerosis ever developed The operation is simple and devoid of danger, and we feel that in all such doubtful cases the patient should have the chance of saving his vision that a sinus operation may offer If in these cases in which the etiology is doubtful the impaired vision is definitely ascribed to multiple sclerosis then there is nothing to do but hope for a spontaneous remission and wait and watch for other symptoms to confirm the diagnosis Due to the development of optic atrophy a delayed sinus operation is of no value

Infection of the Tonsils

A study of the histologic structure of the palatine tonsil offers an explanation for the fact that it is one of the most common locations in the body for a chronic focus of infection The crypts ramify throughout the tonsils and are lined with squamous epithelium The crypt epithelium contains no mucous glands to aid in clearing the crypts of debris or infection The epithelium lining the crypts contains a rich network of blood vessels differing in this respect from the epithelium covering the surface of the tonsil or the surrounding mucosa The microscopic study of several thousand diseased tonsils removed at operation and of a few normal tonsils removed at autopsy indicates that tonsillar infection always begins in a crypt destroys localized areas of the lining epithelium in mild infections and extensive areas in the more virulent infec

tions, thus thrombosing large numbers of capillary blood vessels, the larger collecting veins which lie just under the epithelium and probably also the lymph channels in the vicinity of the crypt[1]. The tonsil is so situated between the pillars of the fauces that it is compressed during the act of swallowing. Elsewhere in the body every effort is made to put an infected area completely at rest, but that is impossible when the tonsils are the seat of the infection. The movement of the tonsil and the surrounding parts during swallowing probably facilitates the spread of infection through both the lymphatics and the venules. This, we think, accounts for the fact that the tonsils are so frequently the portal of entry in such diseases as acute rheumatic fever, bacterial endocarditis, infectious arthritis and glomerular nephritis.

Acute Tonsillitis

The beta hemolytic streptococcus is the organism most commonly responsible for acute and chronic tonsillitis and their complications. Acute tonsillitis is an infectious communicable disease of the lymphadenoid tissue in the nasopharynx and pharynx. The first symptoms may be systemic, such as headache, chilliness, malaise and pains in the knees and back, or may be localized to the throat and adjacent lymph glands. In either case the temperature rapidly rises to 103° or 104° F. (39.4° or 40° C.) and, as a rule, falls to normal on the third or fourth day of the disease. A continued elevation of temperature after the fourth day usually is due to some complication.

The tonsil is rich in lymphatics which drain into the cervical lymph glands at the angle of the jaw. The glands in this locality are enlarged and tender during an attack of acute tonsillitis or naso-pharyngitis and often are palpably enlarged in chronic infections of the tonsils or lymphoid tissue in the pharynx. During epidemics of septic sore throat due to food or milk contaminated with the streptococcus epidemicus, the glands in the neck are greatly enlarged and often suppurate. Enlarged and suppurating glands are regarded as a good prognostic sign. The glands were only moderately enlarged in many of the fatal cases in the Baltimore epidemic of 1913.

Conditions Simulating Acute Tonsillitis. — The exudate of acute tonsillitis is not always confined to the region of the orifice of the crypts, and for this reason an early and accurate bacteriological examination is essential for the diagnosis and treatment. Streptococcus and particularly pneumococcus infections may cause an extensive exudate that simulates diphtheria. That the pneumococcus may be the cause of a severe *membranous pharyngitis* has been known for many years, but the report by Henderson[3], in 1934, of 11 cases with only one recovery indicates the seriousness of this type of infection. All of his fatal cases had a septicæmia. In six cases the pneumococcus type IV

was recovered *from the throat and the blood in four type III the only pa* tient who recovered had a type I infection and Henderson ascribes the recov ery to the administration of serum The onset usually is sudden with an elevation *of temperature chills malaise and headache The pain on swallow* ing is so severe that these patients rapidly become dehydrated The regional lymph glands are enlarged and extremely tender The membrane usually appears on the pharynx or tonsil and may spread to the nasopharynx the soft palate the mucous membrane of the cheeks and occasionally the floor of the mouth and downward toward the larynx A *tracheotomy was necessary* in several of Henderson s cases

Accurate bacteriological information for the differentiation of the various types *of membranous pharyngitis is obtained best from a piece* of the fibrinous exudate removed from the advancing border of the lesion In the older thicker or partially detached pieces of membrane the causal organism is likely to be obscured by the overgrowth *of saprophytes* Richey[4] *in 1932 reported five* cases of pneumococcus pseudomembranous pharyngitis with much the same general and local symptoms as those reported by Henderson All recovered after the local application of a 2 per cent solution of fresh ethylhydrocuprein hydrochloride (optochin)

All of Henderson s and Richey s cases *were* adults but Fox[5] in 1932 reported a similar type of infection in four children A thick fibrinous exudate completely occluded the nasal passages in all of these children a lesion which was not observed in any of the reported cases in adults The onset was sudden with marked toxæmia dehydration and a leucocytosis of from 20 000 to 28 000 Two died and two recovered after a long convalescence and many complica tions His treatment consisted of fluids intravenously the injection of the parent s blood intramuscularly and a 1 per cent solution of optochin locally in the nose and throat

It *is impossible to differentiate diphtheria from* acute membranous tonsil litis by symptomatology and inspection alone A piece of membrane removed from the advancing edge of the lesion should be planted in Loeffler s medium poured in blood *agar plates* and a *smear made and stained for immediate* microscopic examination As a rule however an incubation of six to eight hours on Loeffler s serum is necessary before the diagnosis is certain The possibility of an acute *streptococcus infection in a carrier of non virulent* diphtheria must always be considered

The diphtheritic lesion in the throat usually is bilateral but the membrane may be unilateral and the local *condition simulate* so closely a peritonsillar abscess that diphtheria may not be considered as a possibility until it is too late to save the patient with antitoxin

The following case history illustrates the association of a peritonsillar ab-

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females with an average age of 46 years of Hamburger's[7] 15 cases 14 were women and 11 of these were 40 years of age or over Thompson reports in 1934 40 cases 35 were females and 25 of these were under 40 years of age In 17 of his patients the first symptoms of the disease appeared within one or two days of the onset of the menstrual cycle In 6 there were recurrences which were always associated with the menses

Madison and Squier[8] Kracke and others noted that some patients with agranulocytosis had been taking amidopyrine and some of the barbituric acid derivatives These observations have been confirmed and it is certainly advisable to omit these drugs in all patients with ulcerative mouth lesions Fitz Hugh[10] in 1934 gives the trade name of 31 drugs containing amidopyrine

The etiology is not known and therefore the therapy varies Transfusions x ray treatment over the long bones liver extract intramuscularly and in very severe cases intravenously and pentnucleotide given in the muscles or veins have all been used to stimulate the bone marrow Locally every effort should be made to keep the mouth gums and teeth clean Hamburger sprays the mouth and gums at frequent intervals with a saturated solution of potassium chlorate and applies a copper sulphate solution (10 gr to ounce) to the gums and ulcerated areas four or five times a day

Infectious mononucleosis or glandular fever is an infectious disease in which a membranous tonsillitis or a general pharyngitis is often an early symptom In contrast with agranulocytic angina this disease is rare in individuals over 40 years of age and both males and females are affected in equal proportions In agranulocytic angina there is a paralysis of the structures that form the granular leucocytes while in infections mononucleosis there is a stimulation of the structures that form the lymphocytes This is true in a general way but the variation in the blood count in the reported cases indicates that all blood forming tissues may be affected[11]

The onset usually is associated with fever a sore throat and general malaise but the enlargement of the cervical glands the blood picture and the Paul Bunnell[1] test for the presence of heterophile antibodies in the blood serum definitely establish the diagnosis In some patients with infectious mononucleosis the Wassermann is positive and the lesion in the throat might be confused with syphilis but in these false positive Wassermann reactions the Eagle flocculation test is always negative[12] Differentiation between the throat lesions that may occur with the various blood diseases is not possible without a general diagnostic study

The treatment consists of rest in bed and local care of the mouth lesions There is no specific therapy

Leukæmia is one of the systemic diseases the first manifestation of which may be bleeding of the gums or mucous membrane of the nose

scess and diphtheria Although diphtheria was suspected from the first, a week elapsed before the organisms could be demonstrated in either cultures or smears The patient, C A unit history 50181 is a twenty two year old student nurse who was admitted to the medical service of the Johns Hopkins Hospital on February 27, 1935 complaining of a sore throat and general malaise She was well until 9 a m of the day of admission at which time her throat began to feel tight and swollen Three hours later there was marked pain on swallowing followed in a short time by headache backache nausea and vomiting Her temperature on admission was 103 F the leucocyte count 17 900, of which 94 per cent were polymorphonuclears The physical examination was negative except for the throat condition The pharynx was red, and on the right side between the pillars there was a thick exudate which could be removed easily and no bleeding resulted The cervical glands were swollen and tender on both sides but there was no general glandular enlargement A culture from the throat showed alpha and beta streptococcus but no diphtheria bacilli many fusiform bacilli were seen in smears

On the following day there was a thick grey membrane over the upper portion of the right tonsil and a definite peritonsillar swelling on this side On the third day after onset the peritonsillar abscess was incised and a small amount of pus was obtained The predominating organism was the streptococcus The abscess was again opened on the following day and after this she was able to take fluids by mouth, a nasal tube having been used previously On the seventh day after onset virulent diphtheria bacilli were demonstrated for the first time, and she was then given 10 000 units of diphtheria antitoxin intramuscularly There followed a slow but steady improvement in the general and local condition on the eleventh day after the onset however the soft palate on the right side became paralyzed and eighteen days later a partial palsy of the motor branches to the external pterygoid on the left side was noted These motor palsies gradually cleared up but the persistence of virulent diphtheria bacilli in throat cultures necessitated the removal of her tonsils and adenoids on the sixty-eighth day of the illness She was perfectly well however when discharged from the hospital on May 22 1935

Agranulocytic angina must always be thought of when an inflammatory membranous or ulcerative lesion of any kind is seen in the mouth of an adult female It is rare in children The onset usually is sudden with fever and extreme prostration As a rule a stomatitis or an inflammation of the tonsils or pharynx is present and one of the early symptoms is a sore throat, on on the other hand cases have been reported without the angina

This disease is more common in Germany Austria the United States and Canada than elsewhere in the world Women are affected from 3 to 4 times as frequently as men In Kastlin s[6] series of 43 cases 78 per cent were

There are many reports in the literature of the successful treatment of peritonsillar abscess by excision of the tonsil during the acute stage of infection[1, 16, 17] Although Tito has collected 356 cases thus treated with only one septicæmia we still think it is a dangerous and unnecessary method

The x ray treatment of a carbuncle and other superficial infections often relieves the pain and hastens the healing It might be of equal value in the treatment of peritonsillar abscess provided the irradiation could be applied directly to the inflamed area without first having to pass through the skin and muscles of the neck, and provided we could be certain that no burn of the mucous membrane resulted An x ray burn is worse than the disease

Arthritis —A recent working classification divides arthritis into two clinical groups atrophic (infectious rheumatoid) and hypertrophic[18] The latter form is regarded as a degenerative process and may represent a distinct disease Although Benjamin Rush in 1801 pointed out a connection between infected teeth and general systemic disease with particular reference to joint infection and Billings (191) and Rosenow (1915) forcefully directed attention to this problem again it is not yet known how foci of infection act to produce arthritis Is the joint or periarticular lesion a metastasis secondary to a bacteriemia? Is it due to toxins liberated from a focus of infection? Or could the joint reactions be allergic in nature and represent hypersensitivity of the joint tissues to organisms in distant foci of infection?

Those of us who see large numbers of patients with upper respiratory tract infections feel very strongly that there is a direct relationship between tonsillar disease and arthritis particularly the type that in its early stage affects the periarticular tissues around the small joints in the hands the wrists elbows knees and ankles (infectious arthritis) If there is a history of an infection preceding either the onset or the exacerbation of arthritis and especially if there is clinical evidence of infection the patient should always be given the benefit of the doubt and have all foci adequately treated This is, of course, in addition to general upbuilding measures vaccines etc

Acute Rheumatic Fever — By acute rheumatic fever we mean an acute febrile disease the more common clinical manifestations of which are polyarthritis, carditis chorea and subcutaneous nodules Rheumatic fever is one of the serious complications of tonsillar disease and the question often arises as to the advisability of operative removal of the tonsils and adenoids as a therapeutic measure Opinions differ as to the value of tonsillectomy in chorea or after the cardiac symptoms of rheumatic fever have developed but everyone is agreed that the tonsils may be a portal of entry for the organism or the virus which causes this disease The onset of the initial attack of rheumatic fever and its recurrences is often associated with an upper respiratory tract infection Many patients give no history of a preceding sore throat but those

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Scarlet fever the early lesions of a *syphilitic infection* and *Vincent s angina* must be considered in the differential diagnosis The diffuse redness of the pharynx and soft palate in scarlet fever and the erythema, accentuated in the axillae and flanks should rarely be mistaken for acute tonsillitis

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The recognition of *Vincent s angina* depends on the very slight constitutional symptoms the absence of fever (rarely is the temperature above 101° F (37 7° C), the offensive breath the moderately enlarged cervical glands the swollen, spongy bleeding gums joint pains and the demonstration of the Plaut Vincent organisms in the lesions The ulcerations on the tonsils or gums may be superficial and covered with a diphtheria like membrane or deep with necrosis of the underlying tissues The local application of either powdered arsphenamine chromic acid 5 per cent copper sulphate solution 10 per cent or sodium perborate powder will heal the lesions in the mouth The best therapeutic and prophylactic measure is to visit a good dentist frequently

Complications of Tonsillitis and Nasopharyngitis — In children *otitis media* and a *retropharyngeal abscess* are the common complications of an acute upper respiratory tract infection in adults the complications are more often systemic Infections of the accessory nasal sinuses occur with about equal frequency in adults and children *Sinusitis* in children clears up spontaneously or after the removal of the tonsils and adenoids while in adults local treatment is usually necessary to prevent an acute sinusitis from becoming chronic

Peritonsillar abscess or quinsy is a frequent a very uncomfortable and often a serious complication of tonsillar infection It is thought that this condition is less likely to develop if the patient remains in bed for at least three days after the temperature is normal When the abscess is fully developed, it should be opened by an incision in the most prominent part This is often painful, and it is difficult for the patient to open his mouth but a general anesthetic should never be used when the edema of the uvula and soft palate is sufficient to interfere in any way with normal breathing

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who do give a definite history often state that the rheumatic fever symptoms did not appear until a fortnight later A slight upper respiratory infection is easily forgotten and may precede the attack more frequently than our clinical histories indicate

An analysis of 108 patients with rheumatic fever whose tonsils and adenoids were removed at the Johns Hopkins Hospital[17] is shown in chart I 36 of these have been under observation for more than 19 years and 90 for more than 10 years We find that 86 patients or 79 6 per cent are still alive and 22 or 0 4 per cent are dead Death was due to carditis in 17 (15 7 per cent) and to other causes in the 5 remaining cases In the group of 11 of the young patients in chart I who were observed from 1 to 5 years the death rate is 10 2 per cent That death was not hastened by the operative removal of their tonsils is indicated by the fact that only one of these patients died within less than three months after the operation This patient a child aged 4 years had active chorea but at the time of the tonsillectomy no signs of a heart lesion On the following day the temperature was elevated A scarlatina like rash appeared on the third day and the child died on the fourth day after the operation The autopsy showed fresh vegetations on the mitral and aortic valves Since this fatality in 19 1 we have very positively advised against operation on any upper respiratory tract infection during the acute stage of chorea arthritis or uncomplicated tonsillitis

It is evident from the tabulated results in chart I that the death rate from carditis is much higher in the first five years than it is after this period during the first five years 11 patients or 10 2 per cent died of carditis The cardiac lesions in the patients re-examined after the first five years were for the most part well compensated and the patients were found leading useful and active lives In fact in the entire group of 108 patients only 17 or 15 7 per cent have died of carditis

Coombs[9] in a study of 655 cases of rheumatic carditis very few of whom had had their tonsils removed says If the term cardiac rheumatism is limited to include only those types of the disease in which the diagnosis is plain and incontrovertible from the outset it would be found that of 200 such patients 150 to 160 were still alive at the age of twenty to twenty five more than two-thirds of whom displayed signs of permanent disease of the heart leaving a total of about 50 patients a quarter of the whole group who had lost all physical signs of cardiac disease In our series of 108 rheumatic fever patients in all of whom the tonsils and adenoids were removed as a part of the treatment the average age of the 86 living patients is 26 4 years and only 31 (the 53 with heart lesions (see chart I) minus the 2 dead) or 30 per cent have any signs of an organic heart lesion Coombs finds that more than two-thirds (66 per cent) of his patients still alive at the age of 0 to 25 have signs

Period of Post-Operat. Observation	No. Cases	No. Relapses	Distribution of the Recurrences during the 21 Year Period of Observation (years 1–21)	No. of Patients Living	No. of Patients Dead	The Cause of Death	No. of Carditis on Adm. show	No. with Carditis Last Examination	Death Rate from Carditis
1 to 5 Years	11	11		0	11	11 Carditis	10	11	1027
6 to 10 Years	15	8		10	5	2 Carditis; 1 Pulm. Tb; 1 Erysipelas; 1 P. R. tonsil	6	6	27
11 to 15 Years	36	12		34	2	1 Carditis; 1 Nephritis	14	16	097
16 to 20 Years	30	12		27	3	2 Carditis; 1 Accident	18	12	187
21 to 23 Years	16	4		15	1	1 Carditis	11	8	09%
TOTAL	108	47	20-19-11-9-8-7-9-5-3-2-5-4-1-1-2-2-3-2-3-1-1	86	22	17 Carditis; 5 Other Causes	49	53	1587

Chart I A summary of 108 patients with rheumatic fever whose tonsils were removed as a part of the therapy Only 47 patients had recurrences during the 23 year period of observation

lytic streptococcus is the organism most frequently present in the infections in these cases There are several varieties of the beta hæmolytic streptococcus and Long [3] in 1934 reports the presence of the minute variety in the throat of 33 out of 4 patients ill with glomerular nephritis

Many observers have found that from 40 to 50 per cent of their patients with acute glomerular nephritis get well after the focus of infection has been cleared up In a recent publication [4] from the Medical Clinic of the Johns Hopkins University and Hospital 78 cases of hæmorrhagic nephritis are presented One interesting conclusion reached by the authors is that when nephritis follows a severe and acute streptococcus hæmolyticus infection of the upper air passages some form of resistance often develops which results in recovery from nephritis and the disappearance of the streptococcus If an acute hæmorrhagic nephritis rapidly and completely clears up the kidneys are thereafter relatively immune to damage from subsequent infections such as scarlet fever or an acute streptococcus pharyngitis On the other hand if the beta hæmolytic streptococcus is persistently present in the nose or throat after operation or other therapeutic measures the renal lesion grows progressively worse Operative procedures on infected tonsils or sinuses are often followed by an increase in the hæmaturia albuminuria edema and blood pressure all of these symptoms however usually are transient A careful search for foci of infection is indicated in every patient with glomerular nephritis The most suitable time for operative treatment and the choice of an anæsthetic can best be decided by the internist in charge of the case

Chronic Tonsillitis

The term tonsil usually refers to the palatine tonsils alone The masses of lymph adenoid tissue in the nasopharynx on the lateral and posterior walls of the pharynx and at the base of the tongue are all similar in a structural way to the palatine tonsils All contain lymphoid tissue with germinal centers but the crypts of the palatine tonsils are deeper divide into many branches and following an acute infection are more likely to become the seat of a chronic infection than are the wide mouthed superficial and short crypts in the adenoids and other lymphoid tissue in the pharynx The long ramifying crypts in the palatine tonsils are lined with squamous epithelium No mucous glands drain into the lumen which makes it difficult for the crypt to rid itself of debris and bacteria In acute tonsillitis all lymphoid tissue in the upper air passages is involved but often infection remains in one or more crypts and becomes chronic This occurs most frequently in the palatine tonsils and adenoids but the lymphoid tissue at the base of the tongue which is best examined with a laryngeal mirror is infected more frequently than the text

of permanent heart disease Could this difference be due to the removal of the tonsils and all other evident infections in the teeth or upper air passages in our cases?

Our findings in regard to the disappearance of the signs of cardiac disease agree with those of Coombs since 14 of our 86 living patients, who had clinical signs of heart disease at the initial examination were found to have a normal heart at the last examination The original diagnosis in each was mitral insufficiency never mitral stenosis or aortic insufficiency

The number of patients having one or more recurrences of rheumatic fever, the frequency and the distribution of the recurrences in the years following the operative removal of their tonsils and other upper respiratory tract infections are also shown in chart I In one patient in the 21 to 23 year group, the first recurrence was 21 years after the tonsillectomy A total of 45 patients had recurrences

It is evident therefore that the removal of infected tonsils does not prevent recurrences of rheumatic fever There are either portals of entry, other than the tonsils or the organism or virus causing this disease never disappears after the first infection and re infection is not the explanation for the recurrences On the other hand a large percentage of our group seem to have been benefited by the operation Our advice in regard to operative removal of infections in the upper air passages in rheumatic fever patients is to wait until all acute symptoms have subsided and then remove as thoroughly as possible all infections in the accessory nasal sinuses the teeth, tonsils adenoids and the lymphoid tissue at the base of the tongue

Nephritis — Kidney diseases are divided into 3 great groups 1) Nephrosis, which is characterized by albumin in the urine and generalized edema, but no elevation of blood pressure no blood or cellular casts in the urine and no increase in the blood urea or nonprotein nitrogen 2) the arterio sclerotic or vascular nephritis leading to scarring and contraction of the kidneys, and 3) the hemorrhagic type in which the primary lesion is in the glomerulus, with secondary involvement of the rest of the kidney

In the glomerular nephritis group the onset usually is due to infection in some distant part of the body In a report by Longcope[1], in 1929, the onset of glomerular nephritis was associated with infection in 86 3 per cent of 55 cases In one half of his cases the renal lesion was thought to be due to a tonsillar infection and either a tonsillitis or a sinusitis was the etiologic factor in three fourths of his entire group Loehlein in 1907, described the renal lesions in glomerular nephritis and from his clinical observations concluded that this disease was the direct result of streptococci infection This has been confirmed by Fahr Volhard Longcope and his associates and L W Hill in his studies of nephritis in children All observers have found that the beta hemo-

Other indications for tonsillectomy depend on the study of the individual case especially in rheumatic fever glomerular nephritis infectious arthritis certain infections of the eye the lower respiratory passages and the genitourinary tract As regards hyperthyroidism we feel that if any operation is indicated a partial removal of the thyroid gland will do more to relieve the symptoms of acute hyperthyroidism than will a tonsillectomy Later a tonsil operation may be advisable in order to improve the general health of the patient

The *more important of the contraindications* are 1) An acute respiratory tract infection Although there are many who advocate removal of the ton sils during the acute stage of scarlet fever, acute tonsillitis and peritonsillar abscess we feel that this is a needless risk and it is always advisable to post pone the operation for a month or six weeks after the fever has returned to the normal level

2) The same applies to the systemic diseases which may be due wholly or in part to tonsillar infection It is always safer to wait until the acute symp toms have subsided

3) Unless the indications are very definite the tonsils should not be removed in children under three ears of age

The tonsils and adenoids should not be removed at any time or in any patient unless there is a good indication for the operation If the operation is definitely indicated then all infected tissue including hypertrophied lymph oid tissue at the base of the tongue should be compl tely removed and in such a way that there will be no post operative bleeding or lung complications

Tuberculosis of the Tonsils — The question of tonsillar tuberculosis is in timately bound up with bovine tuberculosis the testing and slaughtering of infected dairy cows and the pasteurization of milk It has been known for many years that the bovine tubercle bacillus may cause tuberculous lymph glands and bone and joint tuberculosis but it is now definitely established that this organism may also cause pulmonary tuberculosis Since 1918 more than 115 000 000 cattle in the United States have been tuberculin tested by the federal and state governments During the year 1932 nearly thirteen and a half million cattle were tested and only 1 9 per cent had a positive reaction in contrast to 4 9 per cent in 1918 Since 1918 the death rate for human tuberculosis has decreased from 128 6 to 56 6 per hundred thousand and the mortality due to tuberculosis other than respiratory has decreased from 5 to 6 4

MacCready and Crowe who reported on tonsillar tuberculosis in a group of patients from Baltimore where the negro population is large found the incidence among the colored race was four times greater than for the whites

Tuberculosis of the tonsils may be primary and due to the ingestion of

books indicate Wietinc [illegible] described a small nodule of lymphadenoid tissue situated in the upper and anterior part of the pyriform sinus which is histologically identical with tonsillar tissue and when infected the symptoms are edema pain on swallowing and the sensation of a large foreign body

The recognition of a chronic infection of the lymphoid tissue in the upper air passages then requires more of an examination than can be made with a spoon and a flash light In some adults and in nearly every child a chronic infection causes the lymphoid tissue in the throat to enlarge, but unless there are other signs and symptoms it is a mistake to assume that every hypertrophied tonsil is infected It may be advisable to remove hypertrophied tonsils and adenoids to get normal breathing to protect the ears and maintain the function of the eustachian tubes or as an important part of the treatment for an infection of the accessory nasal sinuses but as a rule we do not advise their removal, and this applies to children especially, unless a careful history, general and local examination convince us that the patient will be benefited by the operation We know little about the function of the tonsils They do produce lymphocytes and they may be a part of the defense mechanism of the body It is generally thought that involution occurs at the age of 10 to 15 years and that the tonsils and adenoids have performed their main physiologic function during childhood On the other hand, their removal decreases definitely the incidence of scarlet fever otitis and cervical adenitis and many of the complications of the common cold[6] It does not protect against but probably reduces the incidence of, acute rheumatic fever Since it has been shown that the beta hæmolytic streptococcus is the organism responsible for most of the systemic complications of upper respiratory tract infections the mere demonstration in repeated cultures that this organism is present in the pharynx in large numbers is an indication for the removal of the tonsils and adenoids Dean[6] states that many years of observation in two large training schools for nurses have convinced him that the routine removal of the tonsils in probationers is a justifiable procedure Undergraduate nurses are more frequently exposed to respiratory tract infections and take fewer precautions than do other members of the hospital staff Also the nurse who is a 'carrier' of the hæmolytic streptococcus is a great menace to patients with whom she comes in contact, particularly in the children s wards

The local *indications for a tonsillectomy* are 1) repeated attacks of tonsillitis quinsy otitis media and sinusitis 2) chronic carriers of the hæmolytic streptococcus and virulent diphtheria bacilli 3) hypertrophy which interferes with breathing the function of the eustachian tubes and speech 4) small, scarred or partially removed tonsils particularly if the surrounding mucous membrane is hyperæmic the pillars adherent to the tonsil or the glands at the angles of the jaw are enlarged

were nine deaths seven of these were due to tuberculosis and the others to non tuberculous causes Apparently the removal of the tonsils and adenoids did not disseminate the disease and was not responsible for the death of any of these patients One child aged 8 years died six months after the operation of tuberculosis meningitis All of the others died from five to six years after the removal of their tonsils

Of the 63 patients traced 54 are now alive one patient is found to have progressive pulmonary tuberculosis and one additional patient has râles and x ray changes in the lungs but no fever is working regularly and is apparently in good health All of the others are well, and except for calcified glands in the mediastinum and at the root of the lungs no evidence of a tuberculous infection is found on examination

It is well known that a tuberculous infection in a child is less virulent than in an adult This seems to hold true for this group of patients in whom histologic tubercles were found in the excised tonsils or adenoids About 50 per cent of the patients who were between the ages of 15 and 30 years at the time their tonsils were removed are now dead or have signs and symptoms of pulmonary tuberculosis while only one child or 2 per cent of the 50 children observed for fifteen years or more has died of tuberculosis This death was due to tuberculous meningitis

These results indicate that the tonsillar infection in children is a part of the primary tuberculous infection that the disease is not disseminated by the operation under general anæsthesia and that when tubercles are found in either the tonsils or adenoids the prognosis is much better for children under 15 years of age than it is for older children and adults Tubercles in the tonsil of an adult are so frequently secondary to a pulmonary lesion that whenever they are discovered in histologic sections a most careful search should be made for a tuberculous focus elsewhere in the body

All children with enlarged tuberculous or pyogenic cervical glands should have their tonsils and adenoids removed Even when the lymphoid tissue removed from the pharynx shows many tubercles the prognosis is uniformly good as regards the development of pulmonary tuberculosis It is rarely necessary to remove such children from school or do more than regulate their hours of rest and see that they get the proper food

INFECTION OF THE EAR

Otitis media is the most common of all ear diseases This is due to the fact that the eustachian tube affords a direct pathway for infection from the naso pharynx to the middle ear Nasal and pharyngeal infections extend to the middle ear in children more frequently than in adults and every pedia

infected food or milk but it occurs more frequently as a secondary manifestation of a generalized infection Otto[7] found tubercles in the tonsils in 74 per cent of 45 tuberculous cadavers Newhart[8] found that 42 8 per cent of 112 patients with pulmonary tuberculosis had tubercles in their tonsils Very few cases of primary tonsillar tuberculosis have been established by post mortem examination MacCready and Crowe[9] report the incidence of histological tubercles in the tonsils as 3 25 per cent of 2215 patients with no clinical symptoms of tuberculosis in the adenoids in 2 5 per cent of 1000 patients with no clinical symptoms of tuberculosis but in patients with an evident tuberculous cervical adenitis tubercles were found in the tonsils or adenoids in 48 ? per cent These percentages are based on the chance finding of tubercles and not from a study of serial sections and probably represent the lowest estimate of the incidence of tuberculosis of these structures in patients with no clinical evidence of involvement of the lungs

A report was made, in 1924, on the post operative observation of 50 patients with tuberculous tonsils or adenoids[29] Forty of these patients were followed from five to ten years and the remaining ten for at least two years A general physical examination and an x ray of the lungs was made at least once each year during this period Both x ray evidence and clinical symptoms of pulmonary tuberculosis developed in only one patient a child, aged 7 years, who made a complete recovery In four other patients tuberculous changes in the lung appeared two years after the tonsillectomy, but this diagnosis was made on the x ray plate these four patients never had any clinical evidence of pulmonary tuberculosis and subsequent x rays made at intervals of a year showed a gradual fibrosis of the lesions and finally calcification More than 50 per cent of these patients were under ten years of age The low incidence of pulmonary intestinal or other complications during the five or ten year period of post-operative observation the growth appearance and the excellent general physical condition of these children, although many of them originally had tuberculous cervical adenitis or roentgen ray evidence of tuberculous mediastinal glands lead us to conclude that a tuberculous infection of the lymph adenoid tissue in the throat, if not complicated with frequent secondary infection is of distinct value from the point of view of immunity

In a second report in 1935[30] on the post-operative observation of a group of patients whose tuberculous tonsils or adenoids were discovered prior to 1920, we arrived at the same general conclusion i e children with histological tuberculosis of the tonsils or adenoids are found to be healthy and have no clinical evidence of tuberculosis in any part of the body when re-examined from fifteen to twenty years later

A total of 63 patients were traced, with the exception of one patient all have been under observation for fifteen years or more During this period there

artery contains air spaces, and this perilabyrinthine pneumatization may extend far into the petrous tip Gradenigo in 1904 first directed attention to the symptoms of an infection in this part of the temporal bone In his cases there was a purulent otitis, pain in the area of distribution of one or more branches of the trigeminal nerve, due to the proximity of the gasserian ganglion to the infected cells, and a paresis or paralysis of the abducens nerve on the same side Many similar cases have been reported The symptoms of *petrositis* depend on the structures involved in the inflammatory process[3] External rectus palsy is not present in all cases but pain in and around the eye, thought to be due to irritation of either the greater superficial petrosal or the trigeminal nerve is the most common symptom Other complications of an infection in this region may be 1) facial paralysis due to an extension of the inflammatory process to the geniculate ganglion, 2) infection of the superior petrosal sinus which may extend to the cavernous sinus, or through some of the small veins to the brain (A symposium at the 1935 meeting of the American Otological Society on infections of the petrous portion of the temporal bone is published in the Transactions of the Society and in the Annals of Otology Laryngology and Rhinology Dec 1935)

Impaired Hearing —The external auditory canal tympanic membrane eustachian tube the ossicles and the perilymph and endolymph in the cochlea are all a part of the apparatus which conducts sound waves to the end organs of the cochlear nerve (Corti s organ) where they are transformed into nerve impulses Impaired hearing therefore due to a lesion of any of the structures that take part in conduction is called conductive deafness and to a lesion of any of the structures in the cochlea or brain which aid in the perception of sound is called perceptive deafness Acute and chronic infections of the middle ear which impair the movements of the ossicles and obstruction of the eustachian tube are the common causes of impaired hearing in children and young adults while the end results of infections scar tissue and adhesions together with a bony ankylosis of the stapes (otosclerosis) are the common causes of conductive or middle ear deafness in adults Comparatively little is known about the causes of an inner ear or perception deafness Meningitis cerebellopontine angle tumors and some of the infectious diseases notably syphilis and mumps are known causes The diagnosis of the type of deafness and the location of the lesion is made by correlating the history and the results of all methods of examination The audiometer chart records accurately the hearing acuity particularly for the higher frequencies but alone it is of no value for diagnostic purposes The voice and tuning fork tests are of the greatest importance Masking adds to the accuracy of the results of a hearing test By this term is meant the employment of a buzzing noise in one ear when the opposite side is tested The acuity of hearing in a

trician must learn to recognize and treat acute otitis media The common causes of middle ear infection in older children and adults are swimming in infected pools and improperly blowing the nose The nasal passages should be cleared by sniffing rather than blowing Increased intranasal pressure may force infected mucus into the sinuses or eustachian tubes Otitis media is easily recognized by the local and general symptoms and the appearance of the tympanic membrane Properly performed the simple operation of incision of the drum is the most satisfactory procedure in otology Paracentesis should not be done too early in the course of this disease in the ear as elsewhere in the body an acute inflammatory process should be allowed time in which to localize itself before an attempt is made to cure it by surgical incision

The mastoid cells are lined with mucous membrane which is continuous with that of the middle ear in fact these cells the eustachian tube and the middle ear are all parts of one cavity The clinical symptoms of infection in the mastoid as in the accessory nasal sinuses are probably due in large part to obstructed drainage by swollen mucous membrane or thick discharge The mastoid cells are infected early in the course of every acute otitis media, but in the majority of cases the infection clears up spontaneously Symptoms of acute mastoiditis may appear on the second or third day, but a mastoid operation is rarely necessary during the first week of this disease On the other hand an operation is indicated at any time if the toxicity increases, and the temperature remains elevated despite the fact that the drum is widely open and the discharge adequate Mastoid operations during the acute stage, when the infection is not yet walled off are always associated with some danger of a post-operative erysipelas for this reason every care is taken to avoid traumatizing the soft tissues and the wound is left open

A fungus infection of the external auditory canal is common and may be the cause of a thick purulent, foul smelling discharge The usual symptoms are local irritation and itching but when secondarily infected the pain may be severe like that of furunculosis The fungus may invade the tympanic membrane, middle ear and mastoid cells and simulate a chronic pyogenic infection In doubtful cases a correct diagnosis cannot be made without microscopic and bacteriologic studies The treatment of a pyogenic infection is operation but the oral administration of potassium iodid according to the directions given by Chisolm and Sutton[1], is the only measure we know of that will cure a chronic fungus infection

Infection of the petrous portion of the temporal bone is a common route for the extension of a mastoid infection to the cavernous sinus, the meninges and the brain The pneumatization of the temporal bone varies greatly *In some* individuals it is limited to the mastoid process in others the bone surrounding the labyrinth, the upper third of the eustachian tube and the internal carotid

artery contains air spaces, and this perilabyrinthine pneumatization may extend far into the petrous tip Gradenigo, in 1904 first directed attention to the symptoms of an infection in this part of the temporal bone In his cases there was a purulent otitis pain in the area of distribution of one or more branches of the trigeminal nerve, due to the proximity of the gasserian ganglion to the infected cells, and a paresis or paralysis of the abducens nerve on the same side Many similar cases have been reported The symptoms of *petrositis depend on the structures involved in the inflammatory process*[3] External rectus palsy is not present in all cases but pain in and around the eye thought to be due to irritation of either the greater superficial petrosal or the trigeminal nerve is the most common symptom Other complications of an infection in this region may be 1) facial paralysis due to an extension of the inflammatory process to the geniculate ganglion) infection of the superior petrosal sinus which may extend to the cavernous sinus or through some of the small veins to the brain (A symposium at the 1935 meeting of the American Otological Society on infections of the petrous portion of the temporal bone is published in the Transactions of the Society and in the Annals of Otology Laryngology and Rhinology Dec 1935)

Impaired Hearing — The external auditory canal tympanic membrane *eustachian tube the ossicles and the perilymph and endolymph in the cochlea* are all a part of the apparatus which conducts sound waves to the end organs of the cochlear nerve (Corti s organ) where they are transformed into nerve impulses Impaired hearing therefore due to a lesion of any of the structures that take part in conduction is called conductive deafness and to a lesion of any of the structures in the cochlea or brain which aid in the perception of sound, is called *perceptive deafness* Acute and chronic infections of the middle ear, which impair the movements of the ossicles and obstruction of the eustachian tube are the common causes of impaired hearing in children and young adults while the end results of infections scar tissue and adhesions together with a bony ankylosis of the stapes (otosclerosis) are the common causes *of conductive or middle ear deafness in adults Comparatively* little is known about the causes of an inner ear or perception deafness Meningitis cerebellopontine angle tumors and some of the infectious diseases notably syphilis and mumps are known causes The diagnosis of the type of deafness and the location of the lesion is made by correlating the history and the results of all methods of examination The audiometer chart records accurately the hearing acuity particularly for the higher frequencies but alone it is of no value for diagnostic purposes The voice and tuning fork tests are of the greatest importance Masking adds to the accuracy of the results of a hearing test By this term is meant the employment of a buzzing noise in one ear when the opposite side is tested The acuity of hearing in a

child is best determined by masking one ear and testing the other by having the patient answer questions or repeat words Masking is also important when testing bone conduction time The differential diagnosis between a middle and inner ear deafness often depends on the results of the bone conduction test

Shortened or absent bone conduction with good hearing for air conduction is stressed in many text books as an important diagnostic sign of syphilitic involvement of the cochlear nerve Ciocco and Weinstein[1], in 1934 report their observations on a group of 86 patients with a positive Wassermann reaction and other evidences of systemic syphilis They conclude that audiometer and tuning fork tests in patients with impaired hearing due to syphilis differ in no way from those in patients with an inner ear type of deafness due to other causes They find the eighth nerve involved in more than 20 per cent of the patients with latent syphilis and in approximately 70 per cent of those with neuro-syphilis, including tabes and paresis They also find with the vestibular (caloric) test that the incidence of impaired vestibular function is greater in the patients with impaired hearing of the inner ear type than it is in patients with normal hearing In other words both branches of the auditory nerve usually are involved in syphilis of the 8th nerve but an isolated vestibular lesion was found in 33 per cent of their cases A reliable history as to time and nature of onset of symptoms was obtained from 44 patients with nerve deafness thought to be due to syphilis the onset was sudden in 20 and gradual in 24 it occurred before the beginning of treatment in 27 and after in 17

As regards the effect of antisyphilitic treatment on the hearing the conclusions of Ciocco and Weinstein based on the study of 286 patients from the clinic of the Johns Hopkins Hospital differ from those of other observers They find the following 1) With the exception of deafness associated with early meningeal neuro-syphilis antisyphilitic treatment has no effect on hearing either beneficial or detrimental 2) Contrary to the statistics in the literature the development of eighth nerve syphilis is entirely independent of the amount of treatment the patient has received They base this opinion on the hearing tests of patients who had had adequate or inadequate treatment according to the continuous plan outlined by Moore and Keidel Of 228 patients with inadequate treatment an eighth nerve lesion was found in 24 per cent and in 15 5 per cent of 58 patients who had received adequate treatment 3) A diagnosis of neuro-syphilis based solely on impaired function of the auditory nerve in a patient with syphilis is not justified because the results of hearing and vestibular tests in patients with syphilis differ in no way from those in patients with any other type of nerve lesion

Meniere's Disease — The present state of confusion regarding this malady is due to the tendency to diagnose as Meniere's disease or Meniere's symptom complex all patients who have dizziness Another reason for uncertainty in

diagnosis is that neither the etiology, the exact location nor the nature of the pathological lesion is known Meniere s disease rarely is fatal and no histological studies have been reported of both the peripheral and the central auditory and vestibular structures in a patient with characteristic symptoms of this disease Many theories are advanced therefore for the cause, such as vascular spasm of the labyrinthine vessels angio-neurotic edema of the labyrinth faulty water metabolism, gastro-intestinal disorders a toxemia from focal infections occlusion of the eustachian tube and some interference with the circulation of the endolymph and perilymph in the labyrinth With so many explanations regarding the etiology the treatment also is in a confused state and the results are often discouraging to both the patient and the physician

During the past eight years we have made audiometer tuning fork and vestibular tests on 120 patients all of whom had tinnitus impaired hearing and attacks of vertigo which were increasing in frequency and severity These patients were permanently relieved of the most distressing symptom the vertigo by an intracranial division of the vestibular nerve The tinnitus usually is localized on the side with impaired hearing but may be in both ears or heard only in the head The deafness usually is unilateral progressive and has certain characteristics which are of importance in the recognition of the condition we call Meniere s disease

Vertigo may be associated with other conditions but in the disease we are describing the attacks come on suddenly without apparent cause and often during sleep Also without apparent cause there may be remissions with an interval of several years between attacks The vertigo may be preceded by a feeling of fullness in the affected ear loud tinnitus a sensation of floating headache nausea and other auræ and in this way resembles epilepsy There is no uniformity in the description of the attacks even in the same patient This diversity of symptoms in succeeding attacks and the complete absence of vertigo between attacks indicates that the disease could not be caused by any localized lesion in the vestibular nerve or end organs Vestibular tests give us no information they indicated impaired function in 50 per cent of the cases but in the remaining 50 per cent the reaction may be hyperactive or normal

The findings are quite different however when the cochlear nerve is tested In all patients the impaired hearing is of the inner ear or nerve type The high and low tones are affected about equally air conduction is better than bone conduction a vibrating (512 d v) tuning fork held on the forehead i referred to the better hearing ear (Weber test) and bone conduction is markedly shortened or entirely absent in the affected ear The deafnes is progressive and we have seen no patients with remissions during which the hearing returned to normal Subjective improvement in hearing probably is due to temporary diminution or disappearance of the tinnitus

The patient with typical Meniere s disease has persistent tinnitus progressive deafness and attacks of vertigo We have seen patients, however with only one or more of these symptoms who we believe have the same underlying pathology For example a progressive unilateral or bilateral deafness of the inner ear or nerve type without tinnitus vertigo, evidence of focal infection or involvement of other central nervous system structures Other patients have an annoying and persistent tinnitus without vertigo or the signs of nerve deafness Still others have vertigo without tinnitus or deafness Further details regarding medical treatment indications for surgical treatment and operative technique, post-operative symptoms and the ultimate results may be found in the following references[6 7 8 9 10]

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The patient with typical Meniere's disease has persistent tinnitus, progressive deafness and attacks of vertigo. We have seen patients, however, with only one or more of these symptoms who we believe have the same underlying pathology. For example, a progressive unilateral or bilateral deafness of the inner ear or nerve type without tinnitus, vertigo, evidence of focal infection or involvement of other central nervous system structures. Other patients have an annoying and persistent tinnitus without vertigo or the signs of nerve deafness. Still others have vertigo without tinnitus or deafness. Further details regarding medical treatment, indications for surgical treatment and operative technique, post operative symptoms and the ultimate results may be found in the following references[6, 7, 8, 9, 10]

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CHAPTER I-A

DISEASES OF THE BRONCHI

By LOUIS HAMMAN

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7 THACKER-NEVILLE W S Aural vertigo Jour Laryng and Otol 1932, XLVII 533
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Clinically the condition grows rapidly in importance and until these questions of pathogenesis can be settled satisfactorily it seems wise to gather our advancing knowledge under a single descriptive term At present congenital cystic disease of the lungs seems to be the most satisfactory term which has been proposed and the one coming into general clinical use

Incidence

Until recently the disease has been looked upon as a rarity but during the past decade it has been recognized more and more frequently It now bids fair to become a disease of great practical importance on account of the varied and bizarre symptoms it may produce and the ease with which it may be confused with other pulmonary diseases

Although certain descriptions in the publications of older authors may now be recognized as instances of pulmonary cysts Meyer was the first to direct the attention of physicians to the condition In 1859 he reported the postmortem examination of a six months fetus which revealed a small cyst situated near the hilus of the right lung communicating with a bronchus In this country Pappenheimer in 1912 briefly reported the first case but the publication of Koontz in 1925 was the first to attract the attention of American physicians Koontz fully reviewed the literature up to that date and was able to collect 108 cases all from foreign reports A second review of the literature was assembled by Schenck in 1936 and he was able to collect 124 additional cases reported during the intervening eleven years more than half of the cases having been published from the United States There can be no doubt that the disease is often overlooked and the remarkable literary interest in the disease during the past ten years demonstrates clearly that it is not nearly so uncommon as we have supposed heretofore

Pathological Anatomy

The cysts may be small or large single or multiple They may occur in one lung or in both They vary in size from cysts barely visible to cysts so large that they fill the whole of one side of the chest and by pressing upon the mediastinum encroach upon the other side In 228 cases collected by Schenck 82 were solitary or single cysts 146 were multiple The right lung alone was involved in 40 per cent of the cases the left alone is 37 per cent both lungs in 23 per cent Solitary cysts often are formed by the coalescence of many cysts and cysts

CONGI NITAL ABNORMALITIES OF THF BRONCHI

CONGI NITAL CYSTIC DISEASF OI THF LUNGS

The only congenital abnormality of the bronchi which has any clinical significance is the condition spoken of as congenital cystic disease of the lungs Many will dispute the propriety of classifying this disease as a congenital anomaly pointing out that the exact mechanism which pro duces the cysts is not clearly understood and that at least some of them seem to be secondary to well defined pathological conditions There has appeared in medical literature a voluminous discussion of the patho genesis of lung cysts and hardly any two authors agree in all details This uncertainty and confusion has led to the introduction of many dif ferent terms which have been proposed as desirable designations for the disease Among others atelectatic bronchiectasis congenital bronchiec tasis telangiectasis bronchiolectasis fetal bronchiectasis congenital cystic malformation of the lung honeycomb lung cystic fetal bronchial adenoma congenital pulmonary lymphangiecta is To many recent authors the evidence seems to indicate clearly that in most instances the condition begins during fetal life often at an age before the terminal air vesicles are formed Whether the lack of proper development is due to defective constitution of the germ plasm or to environmental factors interfering with orderly g owth cannot be stated with certainty

Pathogenesis

The exact way in which lung cysts develop has not been explained satisfactorily and many conflicting views are entertained Virchow interpreted the case he described as a dilated lymphatic vessel Other observers accept this interpretation for certain cysts in the interstitial tissue which are lined with flat cells resembling mesothelium Most cysts do not have this structure and since the epithelial lining of cysts varies greatly in different parts of one cyst and in neighboring cysts the character of the epithelial lining is not a safe criterion upon which to base views about the origin of the cyst

Stoerk and others contend that the cysts are tumor growths and point out a resemblance to ovarian cysts Projecting into the cysts many tubular outgrowths are often seen and from the character of their histological structure they conclude that they arise from embryonic bronchial tissue Stoerk describes his case as a cystic fetal bronchial adenoma Heller assumes that bronchial cysts arise as a result of faulty development of the alveoli or of congenital atelectasis

Many authors look upon the cysts as the result of inflammatory changes in the lung Sandoz observed multiple cysts in the lungs of syphilitic twin sisters and considers the syphilitic infection responsible for faulty development of bronchioles and alveoli Others have suggested that the cysts are caused by pleural adhesions due to congenital syphilis The association of lung cysts and congenital syphilis may well be an accidental one since the two occur together but seldom

A number of observers argue that the cysts are the result of bronchopneumonia others that they follow infections which lead to stenosis of the bronchi with subsequent bronchiectasis

The view most commonly held is that the cysts result from a developmental anomaly of the bronchi However many careful observers are unwilling to explain all cysts as arising in this way contending that some may come from inflammatory changes others from dilated lymphatics After a very thorough consideration of all the evidence Muller comes to this conclusion From these considerations it follows that often it is impossible to distinguish sharply between those malformations of the lungs which have been described as congenital bronchiectasis cystic lung honeycomb lung cystic degeneration of the lung congenital cystic malformation of the lung fetal atelectasis and aplastic bronchiectasis bronchial and pulmonary adenomata and congenital lymphangiectases of the lung Therefore we are justified in considering them together under the designation congenital cystic malformation of the lungs

which clinically seem to be solitary often are found at the postmortem to be in fact an aggregation of many cysts A lobe of the lung may be riddled with small cysts giving it a honeycomb appearance

Some cysts contain fluid others air still others fluid and air Most cysts in infants contain fluid most in adults contain air This has led some authors to assume that all cysts originally are filled with fluid and that the subsequent contents of the cyst depends upon the character of their lining epithelium whether or not they communicate with a bronchus and if they do communicate with a bronchus upon the character of the communicating channel As a matter of fact when cysts in an adult contain fluid it is impossible to force into them through the bronchus a suspension of opaque material in oil or at necropsy to demonstrate a bronchial communication When there is a free communication with a bronchus through a narrow tortuous channel fluid may escape with difficulty and if as it slowly escapes it is partly replaced by secretion from the epithelial lining of the cyst the cyst may contain both fluid and air The pressure of the air in the cysts has a bearing upon some of the mechanical features of the disease If the communication with a bronchus is open the air in the cyst will be under atmospheric pressure However often the channel of communication is narrow and sinuous and acts as a check valve allowing air to enter easily but to escape with difficulty Under these circumstances air in the cyst may be under high pressure and if the cyst be large or if there are many smaller cysts in one lung the mediastinum may be shifted well over to the other side No doubt increase of pressure in a cyst is often the cause of rupture and may also account for the gradual enlargement of cysts which often occurs even in adult life

The liquid contents of cysts usually is a clear watery fluid sometimes it is rather viscid with mucus when infected it may be purulent and foul smelling

The cyst walls vary a great deal in structure They may resemble tissues derived from bronchi bronchioles atria infundibula or alveoli Most of them contain elements of bronchial structure unstriped muscle elastic and fibrous tissue sometimes cartilage The lining epithelium may be columnar cuboidal or flattened Often ciliated cells are found The different types of epithelium may exist side by side in the same cyst and when cysts are multiple one may contain columnar epithelium another cuboidal and a third flattened The character of the lining epithelium may be modified by the degree of pressure within the cyst The walls of large cysts are thin and rupture easily those of small cysts are thicker and resist perforation

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Clinical Symptoms

Cysts in the lung often give no symptoms and are discovered in adults unexpectedly at autopsy or in a roentgenogram of the chest The occurrence of symptoms depends upon (1) the size of the cysts (2) the pressure relations within the cyst (3) rupture of the cyst (4) infection

It is generally thought that at first cysts are small and that their subsequent size depends upon whether or not they communicate with a bronchus and if they do the degree of patency of the communicating channel Cysts which contain fluid usually are small and even though they may be multiple produce few or no symptoms If they connect with a bronchus freely they contain air but the air is under atmospheric pressure and so long as infection is absent no symptoms arise Occasionally bleeding occurs into a cyst which may be the cause of unexplained hemoptysis When the communication between the cyst and the bronchus is narrow and tortuous the passage may be occluded interruptedly or a check valve arrangement may be formed which allows air to enter but little or none to escape Then rapidly the cyst may become distended soon reach an enormous size and seriously interfere with breathing and aeration of the blood These huge dilated cysts commonly called balloon cysts usually occur in infants only rarely in adults Since the distended walls of the cyst are thin and the pressure within the cyst high they often perforate forming a tension pneumothorax When the cyst or cysts become infected the patients have the usual symptoms of a suppurative lesion Not infrequently the surrounding pulmonary tissue becomes infected and a clinical picture resembling bronchopneumonia develops Later the infection may spread to the cysts and a postpneumonic abscess be diagnosed

Cysts which do not connect with a bronchus and those which communicate freely with a bronchus may persist throughout a long life without giving any evidence of their presence However most patients with cystic disease of the lungs die in infancy or childhood and usually as a direct result of the presence of the cysts and the complications which ensue In a table comprising 60 cases compiled by Adams and Ivanson the age at which the condition was first discovered is given in 59 as follows from birth to 1 month 6 from 1 month to 6 months 4 from 6 months to 1 year 6 from 1 year to 5 years 4 from 5 years to 10 years 4 from 10 years to 20 years 9 from 20 years to 30 years 9 over 30 years 17 The oldest patient in the group was 60 years

Of the 23- cases collected by Schenck the age at the time the condi

tion was discovered is given in 224 as at birth 27 under 1 year 41 between 1 and 15 years 38 over 15 years 118

Schenck arranges the causes of death in the 160 fatal cases as follows

	Infants and Children	*Adults*	*Total*
Congenital cystic disease	56 (60.2%)	36 (53.7%)	92 (57.5%)
Pneumonia	22 (23.6%)	7 (10.4%)	29 (18.1%)
Tuberculosis	2 (2.1%)	3 (4.4%)	5 (3.1%)
Cardiac failure	2 (2.1%)	2 (3.0%)	4 (2.5%)
Other causes	11 (11.8%)	19 (28.3%)	30 (18.8%)
Total	93	67	160

The symptoms most often observed are as follows

	Infants and Children	*Adults*	*Total*
Cough	36	72	108
Dyspnea	42	44	86
Expectoration	16	60	76
Cyanosis	31	19	50
Fever	9	22	31
Malnutrition	12	13	25
Thoracic pain	3	18	21
Hemoptysis	1	20	21
Weakness	2	10	12
Anorexia	5	2	7
Palpitation	1	6	7
Vomiting	5	1	6

The symptoms of cystic disease of the lungs are different in infants and in adults As has already been remarked the huge balloon cysts which often fill the whole of one side of the chest and encroach upon the other *are seldom found in adults The mechanism of their production* is as follows The cysts are formed during intrauterine life and before birth or shortly after a communication is formed with a bronchus This communication may be of a sort which allows air to enter the cyst but not to leave it and increasing pressure in the cyst causes it to dilate The neighboring pulmonary tissue is compressed and becomes atelectatic and in the end may form a narrow band surrounding the cyst or a small mass of tissue accumulated at one point usually about the lower portion of the cyst Often the cyst ruptures and a tension pneumothorax forms

The common symptoms of cystic lung disease in children are dyspnea

cyanosis and cough. Dyspnea often is observed at birth, or it may come on weeks or months later. Sometimes it is so mild as scarcely to attract attention, at other times so severe that suffocation seems to be imminent. Dyspnea often comes in paroxysms and may be accompanied by wheezing resembling an attack of asthma.

When the cyst is large and the pressure within the cyst high, there is cyanosis always, which may be present constantly or come on during fits of crying or coughing.

Cough occurs when there is a communicating channel between the cyst and a bronchus or when there is infection of the surrounding lung tissue and bronchi. Following an attack of coughing the child may bring up large amounts of thick mucoid material indicating that a cyst has ruptured into a bronchus.

In addition to these main symptoms many other accessory symptoms may occur. As a rule the children are poorly nourished, nurse badly and fail to gain weight. A mild anemia may be present. Often there is infection with fever, but usually the fever is not very high since there is little absorption through the cyst wall.

In older children and in adults a balloon cyst seldom develops and therefore dyspnea and cyanosis are not such conspicuous symptoms as in infants. However, dyspnea is a common symptom even in adults though seldom threatening to life. Occasionally a patient may go on into adult life with no symptoms to betray the presence of lung cysts and then suddenly develop intense dyspnea. When this occurs we may predict that a cyst has ruptured and produced a tension pneumothorax. In adults more frequent symptoms are cough, expectoration and pain in the chest, in a word, symptoms due to infection of the cysts and of the surrounding lung tissue. The sputum often is bloody, and at times there is profuse hemoptysis.

Physical Signs

If there is a large cyst or a number of cysts in one lung the chest on the affected side bulges somewhat and the respiratory movements are diminished. The percussion note is a little impaired or dulled and the breath sounds diminished in intensity or suppressed. Rales may be heard over compressed portions of the lung or when there is infection with exudation into the alveoli and bronchi. Large cysts or cysts which have ruptured into the pleura produce the signs of pneumothorax with dislocation of the mediastinum to the other side and flattening of the dome of the diaphragm.

Diagnosis

Small cysts even though multiple which do not communicate with a bronchus may give no symptoms and their presence therefore be un suspected They are revealed unexpectedly at autopsy or in a roent genogram In infants dyspnea not otherwise explained should suggest immediately the possibility of lung cyst in adults any infection with unusual features should arouse our suspicion Since the diagnosis of lung cysts can be made definitely only with the aid of the roentgen ray this method of examination demands especial consideration

When the cyst is filled with fluid it appears upon the roentgenogram as a round or oval sharply defined dark area When the cyst commu nicates with a bronchus it is seen as a translucent area surrounded by a thin sharply defined wall When air and fluid both are present a distinct fluid level may be seen which shifts position with change of posture Sometimes thin trabeculations may be observed traversing the clear cyst When the lung is infected the distinct outlines of the cyst may be ob-scured and the shadow of the cyst merge with the shadow of consolidated lung However even under these circumstances careful inspection of the plate usually will discover the presence of cystic outlines even though they may be hazy

When the lobe of the lung is riddled with small cysts the so called honeycomb lung the condition is difficult to recognize even in the roent genogram and the diagnosis of bronchiectasis may be made

Large balloon cysts may be difficult to distinguish from pneumothorax For the matter of that the two often exist together At times it may be necessary to induce a small pneumothorax before the thin wall of the cyst becomes visible

It is a characteristic of lung cysts that their picture in successive roent genograms remains constant If there is a change in form or density usually the change can be explained by an interpretation of associated symptoms A dense cyst which at a later examination becomes translu cent can mean only that a communication has been established with a bronchus Cysts which rapidly increase in size must be connected with a bronchus through a channel having a check valve action Large cysts which become smaller or collapse must have established a free communi cation with a bronchus Clear cysts which later become opaque must have filled with an inflammatory exudate Hennell reports the interesting case of a man 46 years of age who had had profuse hemoptysis on seven occasions over a period of twenty nine years At the time Hennell saw him he was having his seventh attack The first roentgenogram taken

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of eosinophiles in the blood or a positive complement fixation test will decide in favor of hydatid cyst Successive roentgenograms will distinguish between growing tumors and congenital cysts since congenital cysts do not change their form Thoracentesis with aspiration of the cyst and a careful study of the gross and microscopical features of the aspirated fluid may aid diagnosis

In adults when symptoms arise from congenital cysts they are due almost always to infection The commonest error is to diagnose pulmonary tuberculosis As a rule the roentgenogram is distinctive but not always so In cystic disease of the lungs often there is dense induration and fibrosis of the surrounding lung and the picture may closely resemble that of chronic pulmonary tuberculosis On the other hand an old isolated tuberculous cavity may show little or no infiltration about it and may resemble closely a congenital cyst Recently I saw a woman about forty years of age with a large cavity in the upper lobe of the left lung which the roentgenologists were inclined to consider a congenital cyst until tubercle bacilli were found in the sputum

The next most common error in diagnosis is that of bronchiectasis In the honeycomb lung the distinction often is impossible A history of symptoms beginning almost immediately after birth will suggest a congenital lesion and be in favor of cystic disease a history of symptoms coming on later in life and following an acute pulmonary infection will be in favor of acquired bronchiectasis The bronchial dilatations in honeycomb lung often are larger in the lipiodol roentgenogram than those of acquired bronchiectasis Often the distinction between the two can be made only by an anatomical study of the lung

When cysts become infected the symptoms resemble those of pulmonary abscess When uninfected air cysts also are present the diagnosis may be made from the roentgenogram However when a single cyst or communicating cysts become infected the diagnosis may be difficult indeed at times impossible Cases are reported in which the diagnosis was not suspected until operation was performed

Treatment

In infants and in adults when the symptoms of pressure predominate the first step in treatment is to reduce the pressure Immediate relief usually follows tapping of the cyst However when the contents of the cyst are under increased pressure the bronchial communication acts as a stop valve and after the cyst or associated pneumothorax has been aspirated the pressure again soon rises Therefore the cyst or pneu

demonstrated a number of circular and oval cysts in the lower lobe of each lung A large cyst in the right lower lobe was nearly filled with fluid A second roentgenogram taken three days later demonstrated that the filled cyst had become clear This plainly indicated that hemorrhage had occurred into this cyst and that hemoptysis had come on as the cyst contents were evacuated Subsequently the injection of opaque oil showed that there was a free communication between the cyst and a bronchus

Roentgenograms taken after the intrabronchial injection of iodinized oil reveal many important details When there is an open connection between cyst and bronchus the oil fills the cyst When there is no bronchial connection the oil fills the bronchi surrounding the cyst leaving the cyst itself clear In honeycomb lung pools of oil mark the location of many cysts but the picture is not very different from that of diffuse bronchiectasis

Bronchoscopy often is useful in determining some of the details of cystic disease of the lungs Opaque oil may be injected more accurately through the bronchoscope to discover whether the cyst communicates with the bronchus The communicating bronchus may be located and its degree of patency determined When there is evidence of infection and many cysts are present the exact location of the infection may be found by observing the bronchi from which purulent material is discharged

Differential Diagnosis

The balloon cysts of infancy easily may be mistaken for pneumothorax as may also larger isolated cysts in adults Occasionally it may be necessary to induce pneumothorax to bring into view clearly the thin wall of the cyst Not infrequently cysts rupture into the pleura and produce pneumothorax

Diaphragmatic hernia and eventration of the diaphragm at times may be suspected Roentgenograms taken after the administration of barium by mouth differentiate clearly between the two conditions

Cysts found accidentally in the roentgenogram must be differentiated from dermoid cysts echinococcus cysts and certain solid tumors These cysts and tumors usually are more dense and more distinctly outlined in the roentgenogram than are congenital cysts of the lung Since they arise nearly always from the mediastinum their position in the chest is different from the usual position of congenital cysts At times careful examination of the sputum for hair or the characteristic contents of echinococcus cysts may be helpful The presence of an increased number

either of the chief manifestations of the disease or at least of many special symptoms which frequently occur As illustrations I may mention emphysema atelectasis bronchiectasis abscess tumors asthma pneumonia and tuberculosis The part that bronchostenosis plays in these diseases will be considered fully in the various chapters devoted to them Nevertheless the far reaching importance of the subject makes it desirable to have an independent discussion of its causes and effects

Pathological Anatomy

V Schroetter s classification of the causes of bronchial obstruction as (1) extramural (2) mural and (3) intramural has been followed for decades and is adhered to by Floesser in his excellent review of the subject

Extramural causes of compression of the trachea and bronchi are numerous The commonest of these is enlarged lymph nodes In Hodgkins disease and lymphosarcoma involving the mediastinal nodes pressure upon the trachea or bronchi almost always occurs Older physicians will remember the agonizing death of many patients from suffocation before radiation ameliorated this distressing symptom Nodes enlarged as a result of metastatic tumor deposits may press upon trachea or bronchi often they adhere to their walls invade them and perforate through to the lumen Inflammatory lymph nodes often swell sufficiently to occlude partially the lumen of bronchi the occlusion may be temporary and yet persist long enough to inaugurate serious changes in the distal bronchi which may continue to advance after the compression has been relieved Of all lymph node swellings causing bronchostenosis tuberculosis is the most important from the standpoint of frequency and of the interesting and puzzling clinical symptoms it produces The subject is attracting more and more attention especially from the pediatricians who are publishing an increasing number of observations upon the clinical features Often the nodes become adherent to the bronchial wall ulcerate through and discharge their contents into the lumen

Aneurysm of the aorta is a frequent cause of bronchial and tracheal obstruction When pressure is exerted upon the trachea dyspnea and suffocative symptoms occur when one main bronchus or a lobar bronchus is occluded atelectasis and bronchiectasis frequently follow The symptoms then may be predominantly pulmonary the well known aneurysmal phthisis A greatly enlarged left auricle may compress the left main bronchus

Tumors arising from any of the mediastinal organs may press upon

mothorax cavity must be kept permanently in connection with the surrounding atmosphere This procedure is palliative not curative Nevertheless it may be life saving and allow time for full consideration of the best plan to follow in attempting to eradicate the cyst

Efforts to heal the cyst by collapsing it in the hope that in this way the air will be absorbed and the bronchial communication closed have not been successful Pneumothorax and partial thoracoplasty have been used for the purpose The injection of irritating and caustic substances e g solutions of formalin and of silver nitrate have failed When the cysts are infected simple drainage or marsupialization may relieve the symptoms but permanently draining sinuses remain

Treatment of cystic cavities by the usual conservative methods namely postural drainage aspiration through the bronchoscope the instillation of antiseptic liquids sprays etc are palliative measures which relieve symptoms but leave the underlying condition unchanged

As a matter of fact there is no successful treatment of congenital cysts of the lung other than operative removal Lobectomy and pneumonectomy frequently have been performed with complete and lasting cure Sauerbruch reports operations upon 58 cases of congenital bronchiectasis 6 patients died 51 were cured without a fistula remaining

ALTERATIONS OF LUMEN

Bronchostenosis

Our conception of the nature and the pathological physiology of pulmonary disease has been clarified during the past twenty years by the emphasis which has been put upon bronchial obstruction For this fruitful advance we are indebted chiefly to the surgeons especially to the bronchoscopic surgeons since it is their clinical and experimental observations which have called attention to the far reaching effects of bronchostenosis in determining many of the pathological changes which occur in the lungs and the clinical symptoms and physical signs which mark the progress of pulmonary disease Interest in this matter began when the introduction of the bronchoscope made necessary a careful study of the effects of foreign bodies in the bronchi, in order to insure an accurate diagnosis of their presence and location The knowledge learned from the study of foreign bodies has been extended gradually to explain the origin of many obscure symptoms occurring in other pulmonary conditions and now there is hardly any disease of the lungs in which bronchial obstruction does not play an important rôle in the development

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Tumors arising from any of the mediastinal organs may press upon

the trachea or bronchi for example substernal goitres tumors of the thymus esophageal carcinomata neuroblastomata bony tumors of the spine and dermoid and echinococcus cysts

Inflammatory masses are frequent causes of bronchostenosis I have already spoken of inflammatory lymph nodes how often they compress bronchi and produce puzzling clinical conditions Abscesses from Potts disease from osteomyelitis of the spine from perforation of the esophagus from interlobar empyema and from other locations which perforate into the mediastinum often produce pressure upon the bronchi The scarring left by inflammatory lesions may distort the mediastinum and the bronchi

Mural causes of tracheal and bronchial compression include all those conditions which lead to infiltration of the bronchial walls and narrow the lumen by swelling of the wall by contraction of the wall or by distortion and kinking of the bronchi Here again we encounter inflammatory changes in the lymph nodes as one of the common causes The inflamed nodes adhere to the bronchial walls which in turn become inflamed and infiltrated often with swelling of the mucous membranes and ulceration When the inflammation subsides scarring may constrict the lumen Tuberculosis is the most frequent cause of the lymph node inflammation

Syphilis occasionally occurs in the walls of the bronchi by preference at the point of bifurcation leading to cicatrization and stricture In certain countries e g Austria Poland Latin America rhinoscleroma is a frequent cause

Bronchial carcinoma is perhaps the commonest cause of hilar bronchial stenosis The tumor occludes the bronchus partly by its growth and partly by the inflammatory processes which accompany it The chief symptoms of bronchial carcinoma at least in the earlier stages arise as a result of the bronchial stenosis

A type of bronchial inflammation described as *bronchitis deformans* is characterized by chronic inflammation of the bronchial wall with abundant formation of fibrous tissue and thickening of the wall with distortion of the bronchi It often leads to constriction and sometimes to occlusion of the lumen Males are affected chiefly particularly those working in dusty trades

Occlusion of the smaller bronchi occurs chiefly from intramural causes However certain inflammatory conditions which invade the bronchial walls may cause local or generalized stenosis of the smaller bronchi Pneumonoconiosis may produce peribronchial fibrosis with constriction so also may tuberculosis a combination of the two is a fertile source of such changes A diffuse form of syphilitic bronchiolitis with great thickening and distortion of the walls has been described No doubt

similar though perhaps less extreme changes accompany all forms of chronic bronchitis

Intramural causes of tracheal and bronchial stenosis are those which cause obstruction by the presence of a mass within the lumen Needless to say many causes of bronchostenosis which at first are extramural later become mural and finally intramural For instance an enlarged tuberculous gland may first press upon a bronchus later the bronchial wall may become infiltrated and ulcerated finally the contents of the gland may be discharged into the lumen of the bronchus

Frequent and important causes of intramural stenosis are foreign bodies Other common causes are benign bronchial tumors among which are included the inflammatory granulomata Blood clots not infrequently occlude bronchi and are responsible for certain symptoms which sometimes follow hemoptysis Bronchial carcinoma is a frequent cause of intramural as well as mural obstruction

However the commonest causes and from the standpoint of their far reaching effects the most important causes of bronchial stenosis are inflammatory swelling of the mucous membranes and the lodgement of viscid tenacious secretion It is true that usually these are causes of only temporary occlusion Nevertheless we are becoming more and more convinced of the important role played by temporary bronchial obstruction especially when often repeated in starting bronchial and pulmonary changes which may finally terminate in serious disease

Pathological Physiology

The effects of bronchial stenosis depend upon interference with the free flow of air through the bronchial tubes and the free drainage of secretion These two factors usually work hand in hand to bring about the final pathological condition but often one predominates at least temporarily The conspicuous symptoms of interference with the free flow of air occur chiefly when the larger bronchi are obstructed nevertheless even under these circumstances the results are modified by the stagnation of secretion The conspicuous symptoms of interference with drainage leading as it usually does to infection are observed chiefly when smaller bronchi are occluded Nevertheless accompanying changes of pressure within the bronchi contribute largely to the production of the pathological conditions which finally result The effects of bronchial stenosis vary with (1) the character of the obstruction (2) the location of the obstruction

The obstruction may be complete or partial if partial it may inter

fere equally with the flow of air on inspiration and on expiration or it may interfere chiefly with inspiration or chiefly with expiration Jackson has illustrated these mechanical differences by likening the obstruction to that caused by valves and describes three types of bronchial obstruction (1) stop valve type (2) by pass valve type (3) check valve type

In the stop valve type the bronchus is plugged and air can get neither in nor out When the plugged bronchus is a large one i e a lobar bronchus the air trapped in the lobe is absorbed and the lobe collapses This is the usual mechanism of atelectasis or massive pulmonary collapse

In the by pass valve type the lumen of the bronchus is narrowed air can pass in and out in lessened amounts No striking symptoms accompany this type of obstruction Yet clinically it is extremely important to recognize it since nearly always it is followed by complete obstruction Jackson has emphasized the frequency with which such partial obstruction is accompanied by a wheeze which may be heard at the open mouth but only seldom over the chest

The check valve type of obstruction may allow air to enter but not to escape producing distention or emphysema of the lung or it may allow air to escape but not to enter producing atelectasis or collapse of the lung It is not difficult to imagine the many curious combinations and variations of clinical symptoms which may arise with check valve type of bronchial obstruction The mechanism of these variations has been established by bronchoscopic observation The action of the valve may change quickly and frequently explaining how at one examination we may find emphysema at another collapse Again under peculiar circumstances a tumor or foreign body may so obstruct the bronchi as to produce collapse in one lobe and distention of the neighboring lobe Yet again under certain circumstances e g pedunculated growths the symptoms may be intermittent periods of well being alternating with attacks of emphysema or atelectasis

The location of the bronchial obstruction has an important effect upon its consequences The locations in respect to the character of the consequences are three (1) obstruction of the trachea or both main bronchi (2) obstruction of one main bronchus or of a lobar bronchus (3) obstruction of bronchi smaller than a lobar bronchus

Obstruction of the trachea of such a degree that it can easily be compensated for is soon followed by distension of the lungs This corresponds to the physiological effects of exercise Inspiration is the active part of respiration whereas expiration proceeds passively up to a certain point Therefore the first effect of any increased demand upon the respiration is followed by pulmonary distension When the obstruction

is somewhat more pronounced dyspnea of the inspiratory type develops The exact mechanism by which the inspiratory dyspnea is produced has not yet been satisfactorily explained It seems not to depend upon alterations in the blood gases as was at first supposed Inspiration is prolonged and forcible expiration still proceeds without effort Should the obstruction become still more pronounced necessitating voluntary effort to increase expiration a notable change in the character of breathing occurs Due to the preponderance of inspiration over expiration an increasing degree of pulmonary distension has developed and the point finally is reached when the respiratory and circulatory mechanisms fail We need not inquire closely into the nature of this failure for the details are not fully understood Up to this point respirations have been slow inspiration prolonged deeper and more forcible accompanied by retraction of the intercostal and of the supraclavicular spaces and often by a crowing stridor the time and depth of expiration have been little altered Now usually quite suddenly alarming and distressing attacks of suffocation come on The patient sits up in bed bent slightly forward the head thrown back to stretch the trachea to the utmost he gasps for breath the respiration being shallow and very rapid the pulse is fast and feeble his color gray he breaks out in a cold sweat Many such attacks may recur but unless the obstruction be relieved soon or late the patient dies in an attack

Obstruction of one main bronchus if it occurs gradually may cause no conspicuous symptoms In spite of the collapse of the lung supplied by the bronchus there may be little dyspnea or cyanosis When the occlusion occurs suddenly the symptoms usually are more pronounced When the occlusion is incomplete a valve like arrangement may lead to great distension of the lung and then dyspnea and cyanosis are more conspicuous and in children may be alarming When a lobar bronchus is obstructed leading to atelectasis if the bronchus is occluded to emphysema if the obstruction is partial and so arranged as to allow air to enter but not to pass out no important respiratory symptoms occur Whatever symptoms may be present arise from the nature of the obstruction or from complicating features particularly those of infection

Occlusion of smaller bronchi causes of itself no immediate symptoms unless a large number of the bronchi are plugged Localized bronchiolar obstruction has no effect upon respiration diffuse bronchiolar obstruction causes the most intense dyspnea In bronchiolar obstruction the dyspnea is quite different from that accompanying tracheal obstruction inspiration proceeds quietly and easily but expiration is difficult prolonged and accompanied by diffuse wheezing Occlusion of a bronchus smaller than

a lobar bronchus is not followed by collapse of the dependent lobule Lindskog and Van Allen particularly have emphasized this and have demonstrated the presence of communications between neighboring alveoli which allow a sufficient intralobar circulation of air to prevent collapse of lobules Pulmonary collapse occurs only when a lobar bronchus is occluded Lindskog and Van Allen speak of this intralobar circulation of air as the collateral respiration likening it to the collateral circulation

This brief summary of the mechanical effects of bronchial obstruction upon respiration leaves out of consideration the direct consequences of the simultaneous interference with pulmonary drainage It is surprising to note how long a healthy lobe may remain collapsed and yet when the bronchial obstruction is removed again quickly expand and function normally However soon or late infection occurs and depending upon the type of infection and the detailed character of the obstruction various pathological processes ensue patches of pneumonia abscess gangrene bronchiectasis fibrosis carnification and so on With these results of bronchial obstruction and infection are often mingled those due to the character of the obstructing process e g carcinoma tuberculosis and in final stages the lungs beyond a bronchial obstruction may be veritable museums of almost all known pulmonary pathological processes

Clinical Features

It is impossible to give even a satisfactory glimpse at the varied clinical manifestations of bronchial obstruction without at least a brief account of the diseases in which bronchial obstruction plays an important rôle These matters are discussed more fully in treating each respective disease They are here gathered together merely to give imposing evidence of the constantly increasing importance of bronchial stenosis in our conception of the pathogenesis of pulmonary disease

1 *Atelectasis* — It is now well known that lobar atelectasis is a result of bronchial obstruction Its commonest cause is plugging of a bronchus with viscid secretion as occurs frequently after operation particularly after operation upon the upper region of the abdomen The collapse of a lobe or of a whole lung is not difficult to recognize if we suspect its occurrence and look for the signs which betray it but it is often mistaken for pneumonia or some form of pulmonary fibrosis As a matter of fact atelectasis is the usual precursor of gross pulmonary fibrosis and it may be legitimately questioned if intense scarring of a large area of the lung ever occurs except as a sequel to lobar atelectasis

2 *Emphysema* —The term emphysema has been used to designate many different conditions It is generally employed to designate any form of pulmonary distension though many reserve it for what is also called substantive or hypertrophic emphysema Under conditions when bronchial obstruction is of such a character that air is forced into the lung but its exit is blocked very great acute distension of the lung may result I have not recognized this condition as an important cause of dyspnea in adults but judging from the increasing number of reports I conclude that it is a very important one in children especially in infants The cause of the obstruction usually is pressure by enlarged tuberculous lymph nodes For instance Spivek reports a number of interesting clinical histories The lung supplied by the partially occluded bronchus becomes greatly distended the diaphragm is at a low position the mediastinum is shifted to the opposite side Dyspnea and cyanosis may be intense The attacks subside to recur again or in subsequent attacks complete obstruction of the bronchus may occur and the clinical picture of pulmonary collapse be presented

The mechanism of production of diffuse substantive emphysema is quite different Here the obstruction is in the smaller bronchi leading to greater difficulty with expiration The cause of the obstruction is tenacious secretion in the bronchioles swelling of their mucous linings smooth muscle spasm of the bronchiolar walls and distortion of the walls of the bronchi by inflammatory changes An important part of the mechanism of development of emphysema is that these changes are not uniform throughout the lungs and not constant in position For this reason a considerable degree of localized pulmonary distension may occur without hyperpnea This fact distinguishes the effects of bronchiolar obstruction from those characteristic of asthma in asthma the bronchiolar spasm is more or less uniform throughout both lungs and therefore associated with intense dyspnea

3 *Bronchiectasis* —In the development of bronchiectases we conceive of two processes being at work (1) infection weakening the resistance of the bronchial wall and (2) increased pressure within the bronchus leading to dilatation Bronchiectasis is observed to occur chiefly in atelectatic portions of the lung and in association with dense pulmonary fibrosis Atelectasis itself is indisputable evidence of bronchial obstruction and the view is gaining ground rapidly that dense pulmonary fibrosis nearly always is secondary to bronchial obstruction and atelectasis At autopsy the existence of bronchial stenosis often is demonstrable However bronchiectasis is observed to occur when bronchial stenosis cannot be demonstrated Under these circumstances we are

tempted to conclude that bronchial stenosis at some previous time must have been present even though only temporarily Rapidly accumulating clinical and pathological observations make this assumption not at all unreasonable Andrus in a closely reasoned discussion contends that pressure conditions in the lung tending to dilate large bronchi can occur only in the presence of atelectasis At present we may say that the only proposed cause of bronchiectasis for which there is indisputable evidence is bronchial stenosis Furthermore in instances of bronchiectasis in which bronchial stenosis cannot be demonstrated there is increasing presumptive evidence that at some previous time bronchial stenosis had been present Therefore it seems to me justifiable to hold to the view that bronchial obstruction is a necessary forerunner of bronchiectasis and it is my belief that further observation will firmly establish this view

4 *Pneumonia* — More and more observers emphasize the importance of infected bronchial plugs of mucus as starting points for the development of pneumonia The evidence in favor of this view in post operative pneumonia is very persuasive In the course of pneumonia certain variations in the physical signs for instance loud tubular breathing at one examination completely suppressed breath sounds a few hours later can be explained only by assuming that the bronchus to the lobe has become occluded The spread of pneumonia to an adjoining lobe may be preceded by signs suggesting atelectasis of the lobe It is an interesting and legitimate question to ask if unresolved pneumonia and fibrosis may not always be due to bronchial occlusion the bronchial occlusion being perhaps only temporary

5 *Tuberculosis* — Tuberculosis of the trachea is seldom observed in the absence of patent tuberculosis of the lungs A common site is at the bifurcation of the trachea the tracheal and bronchial involvement often being secondary to a tuberculous lymph node which has become adherent and may later rupture into the trachea or a bronchus The lesions about the trachea or the large bronchi may be infiltrative and need not be ulcerative From these lesions varying degrees of bronchial obstruction may result Enlarged tuberculous glands at the hilum often compress one main bronchus or a lobar bronchus particularly the left lower lobe bronchus

More and more stress is being put upon the important rôle played by bronchial stenosis in determining the character of the pathological changes in the lungs and the clinical symptoms of pulmonary tuberculosis The literature on the subject is growing rapidly It has been pointed out clearly that wheezing in tuberculosis usually is the result of bronchial stenosis and not of asthma Gross fibrosis usually is preceded by ate

lectasis Attacks of acute pulmonary distension often are due to tuberculous nodes Frequently these attacks alternate with attacks of atelectasis Jackson reports an instance in a child aged 20 months The tuberculous mass first caused atelectasis of the right lung by pressure upon the right main bronchus later a wheeze as the result of encroachment upon the left bronchus still later emphysema of the left lung due to check valve obstruction at the same point finally complete closure of the left bronchus and death Adherent tuberculous gland often rupture into a bronchus the immediate mechanical effects may be occlusion of a main bronchus with its usual manifestations Often calcified glands are discharged in this way lung stones are expectorated and profuse hemoptysis may occur If living tubercle bacilli are present in the ruptured caseous gland pulmonary dissemination of the tuberculosis occurs if no viable bacilli are present then the clinical symptoms of epituberculosis come on In either instance the symptoms may be ushered in by atelectasis and indeed atelectasis alone may simulate a spread of tuberculosis or the occurrence of epituberculosis In a word throughout the course of pulmonary tuberculosis bronchial obstruction often enters to color the clinical picture and tuberculosis of the mediastinal nodes is a frequent cause of important clinical symptoms produced by pressure upon the bronchi

6 *Syphilis* —Syphilitic ulceration occurs not infrequently at the bifurcation of the trachea and may lead gradually to obstruction of one main bronchus and then of the other Fortunately this disease seems to become more and more infrequent unless former observers confused it with non specific forms of granulation Instances of mediastinal sclerosis of unknown etiology often are regarded as syphilitic in origin

7 *Bronchial Carcinoma* —The earliest symptoms of carcinoma of the bronchi are cough pain and dyspnea These symptoms occurring at forty years of age or thereafter always should arouse the suspicion of the presence of a carcinoma and demand a bronchoscopic examination The next group of symptoms are nearly always those of bronchial obstruction Again and again at this stage we observe the symptoms of pulmonary consolidation due to lobar atelectasis and often conclude that a large area of the lung has been invaded by carcinoma whereas the growth is a small one occluding a bronchus This fact is very important for in spite of the extensive pulmonary signs the tumor still may be successfully removed at operation

8 The first symptoms of *benign growths* of the bronchus including granulomata may be those of bronchial obstruction The symptoms often may be misinterpreted Particularly characteristic is the repeated

tempted to conclude that bronchial stenosis at some previous time must have been present even though only temporarily. Rapidly accumulating clinical and pathological observations make this assumption not at all unreasonable. Andrus in a closely reasoned discussion contends that pressure conditions in the lung tending to dilate large bronchi can occur only in the presence of atelectasis. At present we may say that the only proposed cause of bronchiectasis for which there is indisputable evidence is bronchial stenosis. Furthermore in instances of bronchiectasis in which bronchial stenosis cannot be demonstrated there is increasing presumptive evidence that at some previous time bronchial stenosis had been present. Therefore it seems to me justifiable to hold to the view that bronchial obstruction is a necessary forerunner of bronchiectasis and it is my belief that further observation will firmly establish this view.

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the lungs are otherwise affected for instance by tuberculosis mild asthmatic symptoms may occur When asthmatic symptoms are pronounced usually both main bronchi are partially occluded The examination of the lungs reveal no abnormal physical signs except perhaps diminution in the intensity of the breath sounds over the affected side

When one main bronchus is completely occluded the symptoms and signs will vary with the suddenness of the occlusion and the character of the occlusion If the occlusion occurs very gradually no conspicuous symptoms may occur although nearly always there is dyspnea Much more commonly the occlusion comes on abruptly even when there has been partial obstruction for some time If the occlusion is complete massive collapse of the lung will occur if it is of such a character that air gets in but cannot get out the lung will become greatly distended With massive collapse there is urgent dyspnea and often violent paroxysms of cough the temperature rises and the leukocyte count increases The affected side is retracted and immobile the mediastinum is drawn towards the affected side the physical signs are those of consolidation or of pleural effusion If the lung becomes emphysematous there is likewise urgent dyspnea and usually severe coughing The affected side is distended but immobile the mediastinum is pushed well over to the other side and the normal lung compressed The percussion note is hyperresonant or tympanitic and the breath sounds suppressed suggesting the signs of pneumothorax The roentgenogram shows an extraordinarily illuminated and transparent lung

When a lobar bronchus is occluded the same results occur as when the main bronchus is occluded but only a single lobe is affected If the lobe is greatly distended the remaining lobe or lobes are proportionately compressed If the lobe collapses it may shrink gradually to a narrow band and the chest be filled by the distended normal lobe or lobes Such compressed lower lobes often are visible in the roentgenogram as paravertebral triangular shadows with the narrow base resting upon the diaphragm and the apex at the hilum of the lung

When the presence of bronchial obstruction is clearly recognized it may be difficult to ascertain the cause of the obstruction In association with infections and particularly after operation or trauma the occlusion usually is due to a plug of viscid mucous secretion Mediastinal masses pressing upon the bronchus must be carefully sought for Foreign bodies carcinoma benign growths and tuberculous glands are particularly frequent causes Bronchoscopic examination is indispensable in reaching a satisfactory conclusion

Occlusion of bronchi smaller than lobar bronchi causes no dramatic

occurrence of what appear to be attacks of pneumonia but which are really temporary atelectasis always affecting the same lobe

Diagnosis

The presence of tracheal obstruction usually is easy to recognize If the obstruction develops gradually there are at first no symptoms when the patient is at rest However with exertion dyspnea comes on When the obstruction is more pronounced the respiratory rate is diminished inspiration and expiration both are prolonged and labored although the accent is usually upon inspiration which often is accompanied by stridor the accessory muscles of respiration are thrown into action and during inspiration there is retraction of the supraclavicular fossæ and the intercostal spaces

It is a matter of the first importance to determine the location of the obstruction because if the obstruction be high tracheotomy may be life saving whereas if it be low tracheotomy is worse than useless Gerhardt years ago called attention to two signs which are helpful in making the distinction namely the position assumed by the patient and the movements of the larynx In laryngeal stenosis the head is thrown back and the larynx moves freely up and down in tracheal stenosis the chin is thrust forward the head bent down and the larynx moves little or not at all Acute stenoses are nearly always laryngeal although a partial tracheal stenosis of long standing which has given only slight symptoms may due to swelling of the mucous membrane or some other cause suddenly precipitate acute and alarming symptoms In all instances of tracheal stenosis the physician will palpate the neck carefully feeling for glandular or other tumors and especially for thyroid enlargement Sometimes palpation of the trachea may allow one to determine the site of obstructon by the localized intensity of the respiratory thrill Retro manubrial dullness may betray the presence of a mediastinal mass and pulsation or a tracheal tug may demonstrate it to be an aneurysm

It is needless to point out the value of radioscopic and radiographic examinations in diagnosis When uncertainty remains a bronchoscopic examination must be made unless the circumstances point clearly to laryngeal obstruction and tracheotomy is urgently demanded

The incomplete obstruction of one main bronchus may produce few and only slight symptoms Usually there is cough sometimes inconspicuous at other times paroxysmal and severe The presence of a wheeze heard at the open mouth is an important diagnostic sign When

the lungs are otherwise affected for instance by tuberculosis mild asthmatic symptoms may occur When asthmatic symptoms are pronounced usually both main bronchi are partially occluded The examination of the lungs reveals no abnormal physical signs except perhaps diminution in the intensity of the breath sounds over the affected side

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Occlusion of bronchi smaller than lobar bronchi causes no dramatic

symptoms unless numerous small bronchi are obstructed The obstruction may be due to mucous plugs or spasm of the bronchial muscles When the obstruction is wide spread dyspnea may be intense the lungs are distended expiration is impeded the expiratory effort being prolonged and forcible and accompanied by sonorous and sibilant râles The symptoms may be intense and paroxysmal as they are in asthma or less severe but more prolonged as they are in various forms of bronchitis If long continued true or substantive emphysema finally develops

Bronchiectasis

Bronchiectasis means a dilatation of one or more bronchi Two main forms are described the fusiform and the saccular Many variations consist of combinations and modifications of these two fundamental forms It is obvious that bronchiectasis cannot be a primary disease but must follow changes in the bronchial walls and altered mechanical relations in the chest brought about by some preceding disease Sometimes this preceding disease dominates the clinical scene and bronchiectasis is an unimportant complication At other times the original disease subsides but the bronchiectasis once begun continues and progresses becomes the cause of persisting symptoms and has the appearance of an independent disease

The disease formerly was considered an uncommon one Newer methods of investigation reveal that it occurs frequently the frequency depending upon the thoroughness with which the clinical investigation is conducted Post mortem statistics indicate that it is found in about 1 5 per cent of routine autopsies Bronchiectasis is predominantly a disease of infancy and early childhood although it may persist throughout a long life If we date the illness from the onset of symptoms we find that about one half of the cases begin during the first decade of life It is unnecessary to comment upon the difficulty in many instances of deciding accurately when the disease did begin and the error this uncertainty introduces into every statistical estimation Frank collected a large number of cases which distributed themselves as follows

First decade	188	Fifth decade	54
Second decade	16	Sixth decade	51
Third decade	37	Seventh decade	56
Fourth decade	39	Eighth decade	60

Of 100 cases reported by Farrell 77 were 30 years of age or younger when they first came under observation 22 in the first decade 28 in the

second and 27 in the third Fifty four dated their symptoms from the first decade of life only 16 were over 30 years of age when the disease first manifested itself Males and females are equally affected In some statistics females predominate in children 202 to 136 whereas males predominate in adults 426 to 282 The predominance of males in adult life is thought to be due to the greater exposure of men to irritating dust infection and inclement weather

When observed at an early stage bronchiectasis usually is restricted to one lung at later stages it often affects both lungs The lower lobes are the lobes nearly always involved It affects the upper lobes alone only rarely and these rare instances usually are secondary to tuberculosis Moreover isolated upper lobe bronchiectasis is a relatively benign disease no doubt due to the ease of drainage especially in the erect position In children the left lower lobe is far more often affected than the right lower lobe in adults this predominance is not so striking In material collected from many sources Duken and von den Steinen found in children that the left lower lobe was involved 204 times the right lower lobe 86 times Of the 149 cases reported by Ballow Singer and Graham comprising mostly adults 74 had involvement of only one lower lobe 40 of the left lower 34 of the right lower In Farrell s 100 cases the left lung was affected 41 times the right lung 23 times both lungs 36 times

It is noteworthy that at least half the cases of bronchiectasis have followed directly upon an acute respiratory infection The infectious diseases of childhood often precede it particularly pertussis and measles Influenza especially in association with pertussis is thought by some to play an important rôle in starting the pathological changes which result in bronchial dilatation In fatal cases of influenza the autopsy often reveals beginning bronchial dilatation The proportionate number of cases developing bronchiectasis seems to vary widely in different epidemics

Warner reports upon 110 cases The disease followed a definite preceding illness in 59 per cent pneumonia 30 per cent lung ab cess 12 per cent influenza 5 per cent pertussis 4 per cent acute bronchitis 3 per cent measles 2 per cent bronchiogenic carcinoma 2 per cent foreign body 1 per cent Of Farrell s 100 cases 20 followed pneumonia 5 influenza 2 bronchopneumonia 18 some acute pulmonary infection diagnosed grip cold specific respiratory infection sinusitis etc 12 one of the acute infections of childhood 4 foreign bodies 3 benign bronchial tumors 2 asthma 9 one or more ca es due to tuberculous mediastinal lymph nodes gassing pleurisy post operative atelectasis post tonsilectomy abscess and septic sore throat

A special word should be said about the frequent association of bronchiectasis and sinus infections. Farrell reports that of 66 patients upon whom roentgenograms of the sinuses were taken only 14 were normal. This proportion is verified by many other observers. Some authors think the sinuses and bronchi are attacked simultaneously by the same respiratory infection; others that a preceding sinus infection is the direct cause of the bronchial infection which leads to bronchiectasis; still others that the sinuses are often infected secondarily by the purulent bronchiectatic discharge. What may be the truth respecting the exact relations existing between sinus infections and bronchiectasis cannot be decided at present. However the great frequency of the association suggests that the relation is something more than accidental. Many authors claim that the symptoms of bronchiectasis are much improved when the sinus infection is thoroughly treated.

Pathological Anatomy and Pathological Physiology

It is customary to distinguish two forms of bronchiectasis, the congenital and the acquired.

The congenital form has been the subject of much discussion. Some pathologists believe it occurs frequently and point to characteristics by which it may be distinguished; others confess to great difficulty in recognizing it and claim if it occurs at all it must occur but rarely. In discussing cystic disease of the lung something has already been said about the great difference of opinion which exists respecting the nature of the cysts and their mode of origin. The matter is hopelessly confused. Congenital atelectatic bronchiectasis is well known. At birth the lungs do not expand uniformly; parts of them may remain collapsed for a long time, indeed may never expand, and parts which at first fill out may collapse later temporarily or permanently. If a sufficient area of lung does not expand the infant dies. This is a well recognized cause of death in the new born, although the exact reason why the lungs fail to expand is not known. General feebleness which makes it impossible for the child to clear the air ways usually is considered the most important cause. It is possible that an imperfect development of the bronchial tree may interfere with expansion. In the present state of our knowledge it is reasonable to assume that the bronchus to the atelectatic portion of the lung has been occluded, perhaps by a developmental error but no doubt far more commonly by bronchial secretion. As I shall point out later atelectasis is the one condition which brings about changes in intrabronchial pressure which tend to blow out the bronchial tubes and

thus facilitate the formation of fusiform and saccular dilatations It may be that these dilatations will not occur unless the bronchial wall is weakened by infection and as a matter of fact at autopsy these cases do show conclusive evidence of inflammatory alteration of the bronchi

It has been demonstrated that at birth the lungs are not fully developed They continue to unfold up to the fifth year or even later The unfolding is not merely an increase of size to match the growth of the child but a progressive development of the lung At birth the interstitial tissue of the lungs is relatively more abundant than in adult life Into this tissue the bronchi radiate from the hilum the terminal bronchioles forming buds which when expanded by the first breath of the child become large alveoli From the peripheral bronchi new bronchioles shoot off which dilate to form new alveoli In this way what at first were alveoli later become bronchioli and what were bronchioli become bronchi many with cartilaginous walls

Some pathologists are convinced that deviations from the orderly course of development is an important factor in the formation of bronchiectasis others for instance Brauer and Wiese think they are of little if of any importance in this relation

The acquired form of bronchiectasis consists of localized dilatation of the bronchi On section the cavities are fusiform or saccular in contour lined by a smooth glistening mucous membrane The widening may be most pronounced at the ends of the bronchi or even restricted to the ends which become club shaped Numerous small saculations may project from the walls of the bronchi giving them a beaded appearance The walls of the dilated bronchi may be eroded and communicate with the surrounding lung tissue or one sac may communicate with another or the bronchiectatic cavity may rupture into the pleural space

In acute cases the bronchi are red and deeply congested the walls thin and soft and the dilated bronchi filled with purulent secretion their walls congested and denuded of epithelium Other bronchi may be lined by a zone of necrotic material in which the original elements of the wall are no longer distinguishable Yet others show more or less destruction of the wall and communicate with small abscesses in the surrounding lung tissue Fissures or tears may occur in the bronchial wall which perhaps facilitate dilatation under appropriate conditions Many bronchi become plugged with inspissated exudate which later may become organized

Evidences of healing may be seen as early as the third week after the infection has begun but usually are not observed until the end of the sixth week At this time varying degrees of bronchial dilatation have occurred Soon the bronchial wall is replaced by highly vascular granu

lation tissue in which remains no evidence of muscle or elastic fibres Low cuboidal epithelium without cilia rapidly covers the inner surface of the bronchial tube

It is well known that most cases of severe bronchitis and bronchopneumonia recover completely and later show no evidence of bronchial dilatation Therefore it is interesting to ask what may be the special factors which decide in a given case whether the inflammation will subside, and healing occur with restitution of the bronchus to a normal condition or will go on to destruction of the bronchial wall dilatation of its lumen and replacement of the wall with fibrous tissue

Some regard the type of infecting organism as the important factor, others bronchial occlusion and the stagnation of purulent secretion There is a difference in the destructive effects of different bacteria upon the bronchial walls In this respect Vincent s organisms supercede all others Smith especially has emphasized their importance in this respect However few observers are willing to agree with Smith that fusospirochetal infection is essential to the development of bronchiectasis As a matter of fact Greey and many other investigators have demonstrated conclusively that bronchiectasis often occurs in the absence of Vincent s infection and that any of the usual organisms found in respiratory infections may alone be concerned Moreover Vincent s infection often occurs secondarily after the bronchial dilatation has occurred

The stagnation of purulent secretion due usually if not always to bronchial obstruction seems to have an important bearing upon the development of bronchial dilatation The subsidence of inflammation certainly is facilitated by efficient drainage and the persistence and spread of infection is furthered by retention of inflammatory exudate filled with bacteria Ulceration and destruction of the bronchial wall is seen often beneath inspissated masses of exudate

In addition to infection which weakens the bronchial wall there must be increase of intrabronchial pressure to blow out the walls and form bronchial dilatations Those who put all the emphasis on infection in the causation of bronchiectasis contend that forces acting normally upon the bronchus during respiration and coughing are sufficient to produce dilatation when the walls are weakened by disease

During inspiration the pressure in the bronchi is somewhat higher than in the surrounding lung tissue during expiration it is a little lower However these differences of pressure are slight and are soon equalized Even with deep breathing the intrabronchial pressure is increased for only a short period at the peak of inspiration and this relatively slight and brief increase of pressure exerts a force not sufficient to bring about

dilatation. Moreover the force during expiration acts in the direction of collapsing the bronchus. Therefore alternately there is a slight tendency to dilatation and to collapse, a state of affairs not likely to lead to permanent dilatation.

But it is claimed that during coughing, especially during severe paroxysms of coughing, the intrabronchial pressure is greatly elevated and dilatation of the bronchi produced which, frequently repeated when the walls are weakened by disease, finally results in permanent dilatation. Andrus has examined these claims in detail and contends that, contrary to common belief, there is only slight increase of intrabronchial pressure during cough.

The inspiration preceding cough is full and quick. Were the bronchial tree rigid, it would lead to temporary but great elevation of intrabronchial pressure. However, it is well known that bronchi normally become longer and wider during inspiration, shorter and narrower during expiration. This mechanism has a wide range of accommodation. Douglas and Haldane have estimated that the functional capacity of the air passages may be increased nearly four times during moderate exercise. Therefore, the increased size of the bronchi will compensate for the increased volume and rate of inspiration without elevating the intrabronchial pressure. The muscular effort of cough is expended chiefly upon a violent expiration, and during this violent effort the pressure within the lung is in the direction of collapsing the bronchi. Clinical experience certainly demonstrates that patients with chronic bronchitis who cough violently and continuously develop emphysema, but they do not develop bronchiectasis except as a result of a complicating pneumonia.

This matter of the dilating force which leads to bronchiectasis when the bronchial wall is weakened by disease has been commented upon and questioned by all authors who have written upon the disease. Medical literature is full of these discussions. Laennec, the first to describe the pathological anatomy of bronchiectasis, ascribed the condition to retained bronchial secretion. Andral in 1827 emphasized the effects of inflammation upon the bronchial wall leading to attenuation and loss of elasticity. Apparently he thought the stress of ordinary breathing sufficient to dilate such weakened bronchi. Reynard in 1838 apparently was the first to describe the association of bronchiectasis and bronchial obstruction. Corrigan, 1838, in his studies on cirrhosis of the lung, noted the frequent association of bronchiectasis with extensive fibrosis. He explained the bronchial dilatation as a result of the pull of the scar tissue. Rilliet and Barthez, 1843, were the first to call attention to the frequent occurrence of bronchiectasis in children and to emphasize the

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two sides The lungs themselves must distend to fill the vacant space and this distension greatly increases the elastic tension which is exerted throughout the lungs The pull of this elastic tension may be estimated by measuring the pleural pressure which often falls to minus 100 cm of water and less Andrus has calculated that the main stress of this pull will fall upon the collapsed lobe and in a direction favorable to dilating the enclosed bronchi

This seems to be a satisfactory explanation of what happens with lobar atelectasis It does not explain the usual assumption that bronchiectasis often follows partial bronchial occlusion It is generally held that partial occlusions often act as valves under some circumstances allowing air to enter but obstructing its exit thus leading to a local increase of pressure manifested by pronounced emphysema of the involved pulmonary lobe Indeed it is reasonable to assume that emphysema will follow a partial obstruction of the bronchus even though there be no valvular action since inspiration is more forcible than expiration However if the lungs are healthy the stress of the increased pressure is absorbed by the lung and the pressure in the bronchi is no greater than in the surrounding alveoli Therefore there is no disproportionate elevation of intrabronchial pressure tending to dilate the bronchi Moreover experience teaches us that conditions of pulmonary distension due to check valve obstruction of a bronchus are of short duration either the obstruction is soon relieved or it becomes complete and atelectasis occurs

The only completely satisfactory and undisputed explanation for the occurrence of bronchiectasis is the presence of bronchial stenosis and pulmonary atelectasis How then shall we explain the many cases in which clinical investigation and post mortem observation fail to reveal evidence of bronchial stenosis? Needless to say it would be gratifying were we able to explain them also as due to bronchial obstruction and atelectasis In the present state of our knowledge this cannot be done with complete justification Nevertheless there is a growing body of indirect evidence which lends some support to this view

Bronchial obstruction often is temporary atelectasis persists for a time and when the obstruction is relieved the lung re-expands and functions as adequately as before All evidence of the obstruction disappears These instances of temporary atelectasis are commonly observed under circumstances which justify the inference that the bronchial obstruction was caused by viscid bronchial secretion for instance after trauma after operation in association with severe respiratory infections However they occur also with foreign bodies in the bronchi and with

role of pneumonia particularly pneumonia complicating measles and pertussis Mendelsohn 1845 contended that cough was the dilating force which produced bronchiectasis when the bronchial walls were weakened by disease Barth 1856 stressed again the importance of bronchial obstruction contending that all the factors previously invoked to explain the development of bronchiectasis were most effective in the presence of bronchial obstruction Biermer 1860 in his comprehensive review of bronchiectasis collected all the views previously maintained and stressed again the importance of bronchial obstruction During the following sixty years these opinions have been reviewed and revised with much discussion and even today the discussion continues However during the past fifteen years accumulating evidence has favored the view that bronchiectasis is caused only by bronchial stenosis

Both clinically and at the autopsy table the relation between bronchial obstruction and bronchiectasis is firmly established Moreover only when the two are found together is the cause of bronchiectasis satisfactorily explained When bronchial obstruction cannot be demonstrated then the cause of the bronchiectasis is a matter of conjecture and dispute Therefore it is important to examine what changes brought about by bronchial obstruction lead to bronchial dilatation If the mechanism is clearly understood it may furnish reasonable grounds for speculation about the causes of bronchiectasis when direct evidence of bronchial obstruction cannot be found

To begin with let us take the simplest form of bronchial obstruction the one about which there can be no dispute namely complete obstruction of either main bronchus or of a lobar bronchus When a bronchus of this calibre is completely occluded the dependent area of the lung collapses in one instance the whole lung in the other the respective lobe To simplify discussion we will assume that one of the lower lobes has collapsed Drainage from this lobe is abolished immediately the stagnation of secretion invites infection and infection once established has every advantage to persist and extend As a result of the infection the bronchial wall becomes weakened We shall not stop to discuss whether or not an uninfected that is a normal bronchus may be dilated if a distending force acts over a long period of time It is sufficient to say that nearly always infection precedes bronchial dilatation As soon as the lower lobe collapses the pressure relations in the chest are greatly altered The chest wall is too rigid to sink in and compensate for the reduction of pulmonary volume The mediastinum is drawn towards the affected side and the diaphragm is elevated but this rearrangement is only a partial compensation since it merely equalizes the pressure between the

of the upper lobe on the other side 4 The left bronchus is narrower than the right and a slight occlusion of the left bronchus will be more important functionally than a similar occlusion of the right

Therefore it is not altogether unreasonable to assume that in many of the cases of bronchiectasis in which no bronchial occlusion can be demonstrated a temporary occlusion may have existed at the time the bronchial dilatation began However experience shows clearly that bronchiectasis often begins with a pneumonic infection and it is hard to believe that occlusion of one or more lobar bronchi has occurred in all of these cases On the other hand most instances of pneumonia resolve uneventfully and we must assume that some special factors are present in the relatively small number which is followed by bronchiectasis This small number we would like to explain as depending partly upon the infecting organism but partly also upon the occurence of atelectasis and of irregular resolution In this field of speculation there are no facts to guide us merely hints and suggestions Lindskog and Van Allen insist that occlusion of a bronchus smaller than a lobar bronchus does not cause atelectasis since *there are communications between the alveoli which furnish a compensatory ventilation and an equalization of pressure throughout the lobe This may be true under ordinary conditions and yet it may also be true that when there is inflammatory exudate in the alveoli the collateral circulation of air may be impeded or suppressed* Be this as it may there is a growing *tendency to emphasize the rôle of* atelectasis in the inception the course and the resolution of pneumonic and tuberculous exudates Many interesting observations are being published which illustrate the important part played by bronchial obstruction and atelectasis in the course of tuberculous disease and it may well be that as our understanding of these conditions advances we will see more clearly into the peculiar relations which lead some pneumonias to terminate in bronchiectasis Perhaps after all occlusion of bronchi smaller than lobar bronchi may under certain circumstances play an important rôle

Symptoms

The symptoms of bronchiectasis vary with the extent of the bronchial dilatatation and the character and intensity of the associated inflammatory changes When the bronchial dilatation is slight for instance consists of clubbing of the bronchial ends there may be no symptoms whatsoever However usually under these circumstances the symptoms *are intermittent or variable depending upon the occurrence of fresh*

swelling of the peribronchial mediastinal lymph nodes. I am much impressed by the rapidly growing number of clinical reports which point to enlargement of the mediastinal lymph nodes as a frequent cause of bronchial obstruction. The suggestion seems altogether reasonable that temporary bronchial obstruction accompanied by infection may lead to bronchiectasis and that the bronchiectasis will persist even though the obstruction may disappear later. Emphysema of the lung surrounding bronchiectatic dilatations is demonstrated frequently at autopsy. So also is dense fibrosis of the lung and pleura. Both of these associated conditions are best explained as the results of pre-existing pulmonary atelectasis.

It is pertinent to call attention again to the frequency with which bronchiectasis begins in childhood. Swelling of the lymph nodes occurs much more readily in children than in adults and in them is conspicuous with respiratory infections and with tuberculosis. That enlarged nodes may compress the lumen of bronchi has been demonstrated again and again, and even though the compression may not entirely close the bronchus, still it may interfere with drainage and form a favorable point for secretion to lodge and thus complete the occlusion.

Delacour in 1894 first pointed out the singular fact that in children the left lower lobe is much more often the site of bronchiectasis than the right lower. This fact has been established by the unanimous accord of all pediatricians who have interested themselves in bronchiectasis. Duken and von den Steinen contend that it occurs nearly three times as often in the left lower lobe as in the right lower. They discuss at length the significance of this disproportion and are convinced that it speaks loudly for bronchial occlusion being the cause of bronchiectasis. The anatomical arrangement of the left bronchus makes it much more liable to compression than the right, and this is the only difference between the two lower lobes that they can suggest. Certainly there is no equal disproportion in the susceptibility of the lower lobes to inflammatory diseases. The facts they point out are these: 1. The right main bronchus is almost a direct continuation of the trachea, whereas the left bronchus branches off at a sharp angle. 2. There is a definite constriction of the left bronchus at a point just before the bronchus to the upper lobe is given off. It is at this point that the left pulmonary artery crosses the bronchus. The authors suggest that the bronchus, held down by the pulmonary artery, may become kinked at this point when the lung is pressed upward as they say it is with coughing. 3. The easy compressibility of the bronchi, especially in children, so that they may be obstructed by light pressure. In infants merely turning the head to one side will cause overdistension

inflammatory reaction has subsided In most instances the infection and inflammation do not disappear entirely but they may be quiescent to flare up at intervals with what appear to be fresh respiratory infections Under these circumstances the patient may have cough and expectoration continuously or he may have cough and expectoration only at times with intervals free from symptoms or again symptoms may be absent for a long time or so slight as hardly to attract notice until some dramatic symptom for instance profuse hemoptysis suddenly occurs as the first evidence of a serious pulmonary disease

The rather common chronic pulmonary infection of the lower lobe which has been designated *chronic non tuberculous pulmonary infection* or *chronic pulmonary basilar infection* is accompanied nearly always by demonstrable bronchial dilatation Indeed there can be little doubt that the *bronchial dilatation* is the *mechanical factor* which harbors the infection and prevents its successful eradication The disease as a rule comes on insidiously there is little fever or other constitutional symptoms of intoxication cough and slight expectoration may always be present accentuated at certain periods or there may be intervals of complete freedom from symptoms alternating with periods of cough and expectoration hemorrhages sometimes profuse occur frequently an associated infection of the paranasal sinuses is very common the condition may persist throughout a life time death may occur from abscess gangrene empyema or pneumonia

In the classical form of bronchiectasis usually there is well defined sacular or fusiform dilatation Cough is severe and expectoration profuse Usually the sacs are emptied periodically of their contents *paroxysms of cough bringing up mouthfuls of purulent sputum* Change of posture often provokes such a profuse evacuation especially in the morning after the night s rest During the day eating may bring on an attack

The sputum is abundant often from 300 to 500 c c in twenty four hours *It is mucopurulent in character When collected in a conical* glass it separates into three layers below a greyish or greyish green granular sediment above mucopurulent masses with shreds hanging down into the middle layer of dirty watery material The lower layer of granular sediment contains numerous *Dietrich plugs* which consist mostly of fatty acid crystals and bacteria At times the sputum has an unpleasant sweetish odor at other times it is foul or fetid The foul or fetid odor is an indication of the activity of fusospirochetal infection

There are no physical signs which are characteristic of bronchiectasis As a matter of fact it is often a cause for surprise that in spite of the

infection Occasionally saccular or fusiform dilatations may for a while produce no symptoms Such dilatations are spoken of as dry bronchiectasis It has been assumed that occasionally bronchial dilatation may occur in the absence of infection and that these cavities may not fill with secretion Clinically we seldom observe a bronchiectatic cavity to persist for any length of time without cough and expectoration The symptoms of bronchiectasis which are considered typical may be absent At a time when diagnosis depended upon the presence of these symptoms bronchiectasis was a rare disease The newer methods of examination which permit us clearly to photograph the outlines of the bronchial tree demonstrate that some degree of bronchial dilatation occurs very commonly Indeed one begins to question if the diagnosis may not be made too lightly and indiscriminately In some instances the symptoms may be mild or intermittent in others they may be extreme and incapacitating

Acute Bronchiectasis — In certain acute or subacute pulmonary infections running a febrile course and terminating in death at the end of two or three months the lungs are found at autopsy to contain numerous bronchiectatic dilatations in addition to areas of bronchopneumonia and scattered abscesses or areas of gangrene The bronchiectatic cavities are filled with purulent material and even the bronchi which are not dilated are deeply congested and contain purulent exudate The illness usually begins with fever cough and expectoration The sputum soon becomes purulent and increases in amount rarely it acquires a foul odor The fever goes to a higher level but remains remittent There is a moderate leucocytosis The patient loses appetite, fails in weight and strength and later shows the symptoms of deep intoxication At first physical examination and the roentgenogram demonstrate the presence of patches of bronchopneumonia in the lower lobes and of diffuse bronchitis Gradually the process spreads irregularly but remains predominant in the lower lobes Usually the diagnosis of tuberculosis is made until the constant absence of tubercle bacilli from the sputum makes this diagnosis untenable Then a non specific pulmonary infection with bronchiectasis may be suspected Fortunately the disease is not a common one Whether it is due to a particular organism or to an unusual reaction to one of the common pulmonary invaders is not known

In children who die of the pulmonary complications of measles pertussis and influenza intense inflammation of the bronchi and bronchial dilatation is found often To this condition also the term acute bronchiectasis may appropriately be applied

Chronic bronchiectasis is the condition which remains after the acute

inflammatory reaction has subsided In most instances the infection and inflammation do not disappear entirely but they may be quiescent to flare up at intervals with what appear to be fresh respiratory infections Under these circumstances the patient may have cough and expectoration continuously or he may have cough and expectoration only at times with intervals free from symptoms or again symptoms may be absent for a long time or so slight as hardly to attract notice until some dramatic symptom for instance profuse hemoptysis suddenly occurs as the first evidence of a serious pulmonary disease

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presence of well developed symptoms the physical examination reveals little that is abnormal The thoracic movements may be restricted on one side the chest somewhat retracted The breath sounds may be diminished in intensity A few moist rales may be heard often only occasionally but when heard always in the same location Any gross abnormalities in the physical signs are due to complicating factors of pulmonary and pleural disease which are present often

Complications

Hemorrhage is a common symptom of bronchiectasis Small amounts of blood occur at intervals almost regularly in the sputum of well defined cases Large hemorrhages come on frequently and are often repeated A large hemoptysis occasionally is the first symptom of the disease The loss of blood may be so profuse as to prove fatal

Suppuration —There is always infection in bronchiectatic cavities and usually of the surrounding pulmonary tissue This infection is a constant menace for there is always danger of the development of pneumonia of abscess of gangrene of empyema Metastatic abscesses occur less commonly and as might be anticipated usually are situated in the brain

Amyloid disease with its characteristic symptoms occasionally comes on *Clubbing of the fingers* is nearly always present in chronic cases and often there is advanced pulmonary osteoarthropathy

Diagnosis

It is interesting to note that Hoover in the first edition of the Oxford System of Medicine published in 1920 begins the discussion of the diagnosis of bronchiectasis with this sentence The writer has never had the opportunity to prove bronchiectasis on any other than inferential grounds In the short space of fifteen years the diagnosis has become a familiar and assured one due to the roentgenological development of bronchography introduced by Sicard and Forestier in 1921 Is it not a matter of wonder to reflect how soon the development of each new method of examination is followed by a rich harvest of fresh knowledge?

A normally functioning bronchus will rid itself of injected iodinized oil in about twenty minutes A bronchus which retains the oil longer than this is regarded as abnormal that is as one with walls altered by disease which has destroyed or impaired the efficiency of the elastic and muscular fibres This is regarded by many as the first stage in the

formation of bronchiectasis although not all such altered bronchi subsequently dilate A definitely ectatic bronchus will retain the oil for a long time often for days and even for weeks

The bronchial dilatations assume various shapes and some authors contend that certain forms result from definite pathogenetic factors and are accompanied by characteristic symptoms For example Bendove and Gershwin describe five types each with certain modifications or subdivisions

1 *The cylindrical form* in which the dilated bronchi filled with opaque oil appear as solid cylinders The cylinders may run to the periphery of the lung or stop abruptly at any point in the lobe Often aneurysmal like pouches appear upon the surface of the tubes at other times the ends are tapered at still other times there are constrictions along the course of the cylinders

2 *The varicose form* appears as swollen cords knotted and tortuous often stretching from the trachea to the smaller bronchioles This type often is associated with dense fibrosis of the surrounding lung

3 *In bronchiolectasis* the dilated bronchioles filled with iodized oil are clustered about empty bronchi which seem to have a normal contour This form is said frequently to follow bronchopneumonia particularly the complicating pneumonia of influenza measles and pertussis

4 In *globular or ampullar bronchiectasis* globules of iodinized oil are scattered throughout the area injected with the oil or are clustered about the bronchus resembling bunches of grapes or raisins Many French authors believe that this type of bronchiectasis is often the result of syphilis and advise antisyphilitic treatment even though the Wassermann reaction may be negative

5 *Primary bronchiectatic abscess* occurs particularly after operations upon the nose and throat It consists of large bronchiectatic cavities filled with pus often intercommunicating The surrounding lung tissue usually is infiltrated and in an ordinary roentgenogram the shadow cast by the consolidated lung may obscure the bronchial dilatation The bronchiectatic cavities clearly appear in the photograph taken after the injection of iodinized oil

Many authors have called attention in plain roentgenograms to the frequent appearance of triangular shadows with a short base lying upon the diaphragm and a long perpendicular side along the margin of the mediastinum When iodinized oil is injected these opaque areas are recognized as collapsed lower lobes with greatly dilated bronchi These are characteristic instances of what is commonly called *bronchiectatic atelectasis*

The bronchoscopic examination alone can seldom decide the diagnosis of bronchiectasis However it always renders great aid in reaching a diagnosis (a) by deciding from which bronchus purulent discharge is coming (b) by facilitating the injection of iodinized oil and (c) by determining in doubtful instances the presence or absence of bronchial obstruction

With these modern methods of examination there is seldom any doubt about the existence of bronchiectasis Confusion may arise with tuberculosis abscess and cystic disease of the lung However bronchography will usually resolve the difficulty

When the presence of bronchiectasis has been established then a possible cause must be searched for Aneurysm or mediastinal tumors pressing upon the bronchus bronchiogenic carcinoma benign tumors the pressure of enlarged bronchial glands tuberculous or syphilitic cicatrices lung stones etc must be thought of as possibilities and excluded In these secondary forms of bronchiectasis the condition causing the bronchial obstruction is the important disease the bronchiectasis the secondary and relatively unimportant disease

Treatment

When bronchiectasis is once developed it is impossible for any treatment to restore the bronchi to a natural state The damage done is irreparable Treatment must be directed either to relieving the symptoms or to radical removal of the bronchiectatic portion of lung As a matter of fact the dilated bronchi of themselves produce no symptoms Not infrequently dilated bronchi cause no symptoms whatsoever and may be discovered accidentally or after the appearance of some dramatic symptom For instance a large hemoptysis coming on in a person seemingly healthy leads to a search for the origin of the hemorrhage and bronchiectasis is discovered unexpectedly Infection of the bronchiectatic cavities and of the surrounding lung tissue is the condition which produces symptoms and therefore treatment is undertaken to control and eradicate the infection The mechanical conditions furnished by bronchiectasis are particularly favorable for harboring infection The dilated bronchi form sacs in which purulent material may accumulate readily especially since destruction of the elastic and muscular tissues of the bronchial wall deprive them of the powerful propelling force supplied by the normal movements and contractions of the bronchi The first problem in treatment then is to facilitate drainage This is best accomplished by what is spoken of as *postural drainage*

To procure a satisfactory evacuation of the bronchiectatic cavities the patient must assume the position most favorable for drainage into the main bronchus and the trachea The position will depend upon the location and direction of the cavity The bronchogram will suggest the desirable position and practice may be necessary finally to settle upon the best position

Postural drainage may be accomplished successfully by bending over the bed or over a chair but a tilting table is more convenient and effective The drainage may be employed continuously or intermittently As a rule intermittent drainage is sufficient After a preliminary period of treatment the patient may be able to empty the cavity three or four times a day and thus avoid cough and expectoration during the intervals

In many mild cases postural drainage is the only treatment needed to relieve all troublesome symptoms Sometimes expectorants especially *potassium iodide* seem to be of added benefit Postural drainage alone will often rid the sputum and breath of fetor If it does not *creosote* by mouth or the intravenous injection of *neoarsphenamine* may be successful

At times postural drainage alone will not completely empty the bronchial sacs Under these circumstances *suction through the bronchoscope is* an added method of great value Simple observations have demonstrated clearly that postural drainage does not empty the cavities as completely as bronchoscopic aspiration Under ordinary circumstances postural drainage is sufficient to relieve symptoms and when it is sufficient in *this respect no other treatment is required In case the symptoms are* not satisfactorily relieved then bronchoscopic aspiration should be employed Whether or not drugs directly injected through the bronchoscope are of value is not yet definitely settled Many authors contend that the repeated *injection of lipiodol* is very beneficial

Methods employed to compress the lung have been of relatively little value *Only an occasional case is helped by pneumothorax treatment Phrenicectomy* has been disappointing I have seen a few patients somewhat relieved of cough but have never seen striking benefit

Thoracoplasty sometimes is followed by improvement but it does not cure the condition and seems to be no longer warranted except perhaps in an occasional case since lobectomy and pneumonectomy are hardly more formidable procedures

If a patient s symptoms are not satisfactorily relieved by postural drainage and bronchoscopic aspiration then the advisability of performing *lobectomy* or *pneumonectomy* must be considered seriously Up

to the present time the results of operation have been excellent and with improving operative technic they will no doubt be even better in the future Acute cases with fever and severe constitutional symptoms are not suitable for operation Chronic unilateral cases are the ones usually selected However we may be prepared to see both lower lobes safely removed at successive operations Already this has been accomplished in some patients

Unfortunately we know of no way to *prevent* the development of bronchiectasis Nevertheless certain relations suggest themselves which may be of value in this connection Growing expertness in the diagnosis and removal of foreign bodies has no doubt prevented the formation of many bronchiectatic dilatations Perhaps the more and more frequent use of the bronchoscope in all pulmonary affections may lead to the earlier recognition of bronchostenosis and thus prevent the serious complications which may follow For instance the early discovery and removal of benign growths and granulomata will prevent the development of another number of cases of bronchiectasis The prompt detection of atelectasis and the employment of treatment appropriate for the condition may prevent still others Control of the infections of childhood likewise will be efficacious

In discussing the pathogenesis of bronchiectasis I emphasized sufficiently the important rôle of pulmonary infection Anything that might be done to prevent pulmonary infections or to control their virulence would be helpful Perhaps a longer or more guarded convalescence in childhood might accomplish something Many observers advise the early use of bronchoscopic treatment when cough persists after recovery from an acute respiratory infection Others emphasize the importance of treating thoroughly the infections of the upper respiratory passages which very often are associated with recurring pulmonary infections How efficacious these methods may prove to be we cannot at present tell

TUMORS

Malignant Tumors

It is now generally conceded that nearly all primary carcinomata of the lungs are bronchial in origin *bronchiogenic carcinoma* These growths are fully considered under Tumors of the Lungs in the chapter on Diseases of the Lungs to which chapter the reader is referred (see Chapt III *Vol* II)

Benign Tumors

Until the advent of bronchoscopy benign tumors of the bronchi were considered to occur only very rarely and they were never diagnosed during life In the classical volume of Fraenkel on Diseases of the Lungs published in 1903 they are referred to only casually as occasional causes of bronchial obstruction Lord in his book on Diseases of the Bronchi Lungs and Pleura published in 1915 merely notes their rare occurrence in the volume on Diseases of the Respiratory Tract in The Special Pathology and Therapy of Internal Diseases Edited by Kraus and Brugsch in 1924 they are not even mentioned nor does Hoover consider them in discussing diseases of the bronchi in the first edition of these volumes published in 1920

Therefore benign tumors of the bronchi furnish for discussion a new clinical topic introduced to our attention a little over thirty years ago when the bronchoscope first came into use and generally recognized as a matter of practical importance only during the past fifteen years The first report of the correct diagnosis and successful removal of a benign bronchial growth by the aid of the bronchoscope came from Von Eicken in 1907 During the past ten years many authors have reported upon series of cases Jackson 1932 36 cases observed by himself Wessler and Rabin 1932 17 cases from Sinai Hospital New York Morlock and Pinchin 1935 9 cases from Victoria Park Hospital London there is a large number of descriptions of one or two cases Even a superficial review of the literature would furnish over 100 cases upon which to base a summary of the clinical manifestations of this interesting and important condition

The practical significance of the disease is attested by the following established facts

1 Since we have become accustomed to look for benign tumors under appropriate circumstances and since they can be diagnosed easily by the microscopical examination of particles of the growth removed through the bronchoscope we have found that they occur much more frequently than we had supposed heretofore Kramer and Som report that since the introduction of the bronchoscope they have examined 332 cases of carcinoma of the lung During the same period they have encountered 23 cases of benign tumor Therefore benign growths form six per cent of all bronchial and pulmonary tumors Morlock and Pinchin have examined 150 cases of new growths of the bronchi and lungs among which nine or six per cent have been benign

2 It is impossible to diagnose benign tumors without the aid of the

bronchoscope although experience has taught us to suspect their presence when certain characteristic symptoms occur

3 When the disease is diagnosed at an early stage before serious complications have come on the prospect of complete cure is excellent

4 Although the tumors as tumors are benign and do not threaten life by invasion or metastasis still they are extremely malignant in the sense that when they are neglected the grave complications of bronchial obstruction soon or late set in and lead on rapidly to death

Pathological Anatomy

Jackson and Jackson report having encountered the following types of benign bronchial tumors angioma hematoma adenoma myoma myxoma papilloma fibroma fibro lipoma edematous polyp myomatoid edematous polyp lymphoma lymphangioma lymphadenoma lipoma ecchondroma osteoma, chondrosteoma retention cyst amyloid tumor aberrant thyroid tumor specific granuloma and non specific granuloma

Speaking strictly the granulomata are not tumors but they cause precisely the same symptoms as benign tumors and therefore it is a practical advantage to group them with the tumors More than this inflammatory reactions often occur about tumors and it may be difficult to decide whether tissue removed through the bronchoscope is a tumor with inflammatory reaction or an inflammatory granuloma Granuloma is a common type of obstructing mass and it is probable that many granulomata have been diagnosed as tumors After all has been said the distinction is of little practical consequence

The histological characteristics of the many types of bronchial new growths are not so clearly defined and distinctive that the differential diagnosis is easy As a matter of fact it is extremely difficult, and it happens not infrequently that one pathologist will place the specimen in a certain category and another pathologist in a different one These disputes when they occur are only of academic interest for the methods of treating all forms of benign bronchial tumors is the same and the results of treatment equally good in all forms On the other hand what does greatly concern us is the decision whether or not the tissue shows microscopical evidence of malignancy This decision is not always easy to make Sometimes repeated examinations must be made of bits of tissue removed from different parts of the tumor Even then erroneous opinions have been recorded Some tumors which eminent pathologists thought to be malignant have turned out to be benign and others

pronounced to be benign have later proved to be malignant Indeed there is evidence to support the view that tumors at first benign may *after many years become invasive A safe practical attitude towards* these matters is to consider a tumor benign if pathologists agree among themselves that it is benign and to regard it as malignant if they agree that it is malignant however if there is a difference of opinion or if the question of malignancy is doubtful then the clinical manifestations must be carefully considered before reaching a conclusion

Symptoms

The symptoms of benign bronchial tumors must be divided into two groups 1 those which occur before bronchial obstruction has developed and which are due to the presence of the tumor 2 those which follow bronchial obstruction and are due directly to the bronchial obstruction

It is interesting to note how long benign tumors may be present without giving any noteworthy symptoms Often the sudden onset of bronchial obstruction is the first clinical manifestation This is true particularly of pedunculated papillomata which may cause no inconvenience whatsoever until they fall into the mouth of a bronchus in such a way as to occlude it The symptoms which may occur with a benign tumor before it has caused obstruction are cough hemoptysis wheezing and paroxysmal dyspnea

Cough is seldom very annoying although it is the most constant complaint It is a dry irritative cough with no expectoration or at most a little mucoid secretion

Hemoptysis or at least bloody sputum occurs in about eighty per cent of the cases Sometimes there is recurring hemoptysis of relatively large amounts 100 to 200 c c but more often only bloody sputum These cases are puzzling because the physical examination and the roentgenogram reveal no evidence of pulmonary disease As a rule the bleeding comes on suddenly and stops just as abruptly it is not followed by a day or days of bloody sputum as usually is the case in pulmonary tuberculosis In women bloody expectoration from a benign tumor may recur at each menstrual period

Jackson lays great emphasis in diagnosis upon hearing a wheeze at the open mouth Sometimes the wheeze may be heard at a localized area over the chest wall If it is heard constantly when the patient assumes a certain position and disappears with change of posture then the presence of a pedunculated tumor is highly probable Wessler and

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Rabin describe attacks of dyspnea coming on similarly with change of posture which have the same significance

When the bronchus has become occluded by the tumor the usual symptoms of bronchial obstruction occur At first there is collapse of the portion of the lung supplied by the bronchus later, when infection has set in there may be purulent bronchitis bronchiectasis abscess empyema gangrene and induration of the lung For a time the bronchial obstruction may be intermittent and recurring attacks of pulmonary collapse which usually are thought to be pneumonia are separated by periods of well being Needless to say it is characteristic that the pneumonia in each attack always occurs in the same location

Diagnosis

As may be concluded from what has been said benign bronchial tumors produce varied and colorful clinical pictures In the early stages the symptoms may be so trivial as hardly to attract attention Fortunately in most cases there is at some time hemoptysis or at least bloody expectoration and when this occurs it is not overlooked by the patient The physician at once suspects tuberculosis and properly so since tuberculosis is the commonest cause of blood spitting However if the examination fails to disclose any conclusive evidence of the presence of tuberculosis the possibility of the symptoms being due to tumor malignant or benign must be considered seriously and a bronchoscopic examination never omitted A dry irritative cough especially when a wheeze can be heard at the open mouth should always be thoroughly investigated in the same way

With the onset of bronchial obstruction more dramatic symptoms occur which often are of such a nature as to distract our thoughts from the possible presence of a benign tumor During the early stages the obstruction may be intermittent the tumor falling into a bronchus and later out again If the bronchus is occluded only for a brief time attacks of dyspnea sometimes with wheezing come on A diagnosis of asthma might be made from the history although the sudden onset of symptoms their short duration and abrupt termination sometimes with change of posture should arouse our suspicion If the bronchial obstruction lasts for a longer time pulmonary collapse occurs with fever prostration leucocytosis signs of pulmonary consolidation and so on It is very easy under the circumstances to make the erroneous diagnosis of pneumonia of grip or of tuberculosis I recall such a humiliating experience In March 1927 I saw in consultation a man 40 years of age who four or

five days before while running to catch a train had been seized suddenly with a severe paroxysm of cough followed by increasing dyspnea Later there was fever and moderate prostration The left side of the chest was retracted and moved little the heart was drawn well to the left and over the left lung there was dulness and suppressed breath sounds There was a history of the patient having had a similar attack three months before which had been diagnosed grip Very stupidly it seems in retrospect I interpreted the signs to indicate extensive fibrosis of the left lung and suggested tuberculosis as the likely diagnosis I saw the patient but the once and did not know that a roentgenogram taken a few weeks later after he had recovered showed the lungs to be perfectly normal In a subsequent attack the correct diagnosis was made by another physician Ashbury and Habliston have both reported the case

After the bronchial obstruction has lasted for some time infection follows and then the clinical picture is that of suppurative pulmonary disease For instance when a patient enters the hospital with empyema who will suspect that a benign tumor plugging a bronchus is the cause? And yet even in these late stages a thoughtful consideration of a carefully taken history may give the clue But alas at this time the damage is irreparable What we must aim to do is to make the diagnosis at an earlier stage when appropriate treatment usually is curative

Now that we are becoming familiar with the clinical manifestations of benign bronchial tumors we suspect their presence more and more often and diligently search for them The roentgenologists are more proficient than formerly in distinguishing pulmonary collapse from other forms of consolidation though often there is still uncertainty The bronchoscope is the one reliable means of diagnosis and since bronchoscopy is being generally employed in the investigation of all pulmonary and bronchial conditions of obscure origin there is no doubt that benign tumors will be detected more and more frequently and only neglected cases will go on to develop the late and serious symptoms of bronchial obstruction

Treatment

Benign tumors are removed satisfactorily through the bronchoscope A number of successive operations may be necessary The tumors often recur and therefore after they have been removed the site must be examined at intervals The results of operation undertaken at an early stage are excellent After bronchial obstruction has occurred and a

lobe of the lung has been collapsed for some time removal of the obstruction may be followed by expansion of the lobe and return to normal conditions Even when suppuration has begun and abscess or bronchiectatic cavities have formed the patient s condition may be improved and the local symptoms ameliorated

In certain instances in which the tumor is located in a small bronchus deep in the substance of the lung lobectomy may be required

DISEASE DUE TO INFLAMMATION

Acute Bronchitis

Acute bronchitis is rarely if ever an independent disease Nevertheless it so often occurs with other diseases that it is one of the commonest conditions the physician encounters and is called upon to treat There is scarcely a specific infection with which it is not frequently associated and it is a striking complication of many virus infections for instance measles influenza small pox chicken pox the common cold Bronchitis often is the forerunner of pneumonia both lobar and lobular many observers believing that bronchial secretion occluding the smaller bronchi facilitates infection of the lung Irritating dusts and vapors are further causes of acute bronchitis

The predominant cause of acute bronchitis is the common cold indeed it is an integral part of the reaction which is called a cold Now that we know the common cold is a virus infection we understand its ready communicability It is no longer pertinent to search for the specific bacterial cause of acute bronchitis Innumerable studies in the past have demonstrated that many different bacteria may be present the group comprising chiefly those usually found in pulmonary infections namely the pneumococcus the streptococcus the influenza bacillus and the staphylococcus These bacteria bear the same relation to the complications and sequelæ of the common cold that they do to those of influenza Both influenza and the common cold would be relatively benign infections were it not for their singular influence in reducing the body s resistance to bacterial invasion The common cold subsides in a few days but the effects of bacterial invasion chiefly in the form of bronchitis may persist for weeks thereafter

In bacterial infections the bronchitis which so frequently accompanies them may be due to the specific bacterium or to another organism Bronchitis to a slight or more severe degree is nearly always present in the early period of typhoid fever and in many instances the typhoid

bacillus can be cultivated from the sputum Likewise the diphtheria bacillus may provoke bronchitis when there is a diphtheritic infection of the pharynx or larynx The plague bacillus may be found in the bronchial secretion of patients with plague the anthrax bacillus in anthrax the malleus bacillus in glanders In other infectious diseases the cause of the bronchitis may be a secondary invader Bronchitis is a frequent occurrence during the secondary stage of syphilis due to an efflorescence upon the bronchial mucous membrane of the patches characteristic of the activity of the *Treponema pallida*

Pathology

In the earliest stage of acute bronchitis the mucous membrane is red dry and glazed A little later the inflamed mucous membrane swells and secretes clear mucoid fluid containing a small number of desquamated epithelial cells At this time the sputum consists of clear glairy mucoid masses Still later leucocytes appear in the secretion and streak the mucoid masses with yellowish or greenish purulent flecks or bands In mild cases the inflammation then subsides the secretion diminishes and again becomes mucoid the swollen mucous membrane shrinks and with the disappearance of congestion the normal pink color returns In more severe cases the secretion becomes increasingly purulent and the expectoration of thick mucopurulent masses may persist for a week or longer before the inflammation begins to recede

In mild cases the inflammatory process is limited to the trachea and large bronchi a condition usually referred to as *tracheobronchitis* In children particularly but also in adults the inflammation often extends to the smaller bronchi Swelling of the mucous membrane of small bronchi temporarily may occlude them and plugs of tenacious secretion may obstruct larger bronchi In children these obstructions may produce areas of atelectasis or of emphysema depending upon whether the bronchus is completely or partially closed

Symptoms

It is difficult to decide what part bronchitis may play in causing the fever headache and general malaise which so frequently accompany it It is my impression that these symptoms usually are due to the specific infection which the bronchitis complicates because the bronchitis may persist or seem even to grow worse after the fever and other constitutional symptoms have subsided This is certainly true of the common

cold It is likely that the usual form of tracheobronchitis produces no constitutional symptoms but that fever and general malaise may accompany an extension of the bronchitis to the smaller tubes

The local symptoms of bronchitis are a matter of common experience to everyone At first there is an unpleasant sensation of dryness and tickling in the pharynx and trachea which often provokes an harassing paroxysmal cough without expectoration Soon secretion begins and quickly becomes more abundant At this time the irritative cough disappears the cough becomes less annoying and now produces at first mucoid masses later mucopurulent sputum Cough and expectoration last a week or ten days and then diminish although some cough with clear mucoid sputum may persist for another week or two

There is always a degree of dyspnea not noticeable when the patient is at rest but becoming more or less prominent on exertion often accompanied by wheezing No doubt the dyspnea is due to occlusion of many small bronchi by the swollen mucous membrane and by plugs of tenacious secretion

Physical Signs

There are no physical signs of bronchitis other than the presence of sonorous and sibilant rales These may be numerous or entirely absent It has been my experience that often rales may be heard when the patient lies down even though they are not heard when he sits up It is characteristic that the rales come and go at one time being heard here at another in a different location at still another elsewhere It is to me a matter of recurring surprise to see patients with harassing cough and profuse mucopurulent sputum and yet not be able to find a single rale nor any other abnormality on physical examination In addition to a few generally distributed sonorous and sibilant rales one may hear many medium and fine moist rales usually restricted to one lung or to a single lobe This condition is met with particularly in children Under these circumstances we conclude that the finer bronchi have become involved As a matter of fact there is then nearly always exudation into surrounding alveoli that is patches of bronchopneumonia This is particularly true in the condition spoken of as *capillary bronchitis* which affects chiefly the aged young children and those enfeebled by disease Fine moist râles are heard throughout both lungs there is fever prostration cyanosis dyspnea cough and abundant mucopurulent expectoration Even though the physical examination may reveal no areas of consolidation still scattered patches of bronchopneumonia are always present

The condition is more appropriately grouped with bronchopneumonia than with bronchitis

Treatment

The treatment of acute bronchitis is extraordinarily simple There is only one treatment that is at all efficacious namely to remain in bed until the symptoms have subsided To many this simple and pleasant remedy seems an unwarranted heroic restriction for such a minor ailment and so most of those afflicted struggle on with their accustomed tasks through a dispirited week or two Nevertheless to those unfortunate sufferers who after each cold develop bronchitis which lasts for weeks or months ten days in bed begun at the onset of a cold is a great boon In the long run it prevents months of discomfort and may actually save time lost from work Perhaps it may even be more salutary in less obvious ways for an established chronic bronchitis often follows repeated colds with protracted bronchitis and to be spared the unpleasant symptoms of chronic bronchitis and the risk of developing some of its disabling complications is worth a greater sacrifice than the irritation of spending a few days in bed

All other treatment of acute bronchitis is symptomatic Every layman has his favorite method for breaking up a cold These methods are numberless some inconvenient others mild forms of torture still others soothing and pleasant None successfully accomplish the purpose at least not uniformly as is evident from their great number and the extravagant claims made for each Those physicians whose tough philosophy of life inclines them to the view that no good can be attained without bodily pain and discomfort will discipline their patients with cathartics steaming foot baths followed by cold rubs profuse sweats induced by drinking large quantities of hot flaxseed lemonade the application of irritant mustard plasters etc etc whereas those of a softer mold and hedonistic tendencies will aim to soothe the patient with mild sedatives and a pleasant punch or toddy I have no doubt both methods are equally efficacious

It is entertaining to observe the punctilious attention bestowed by older physicians upon the therapeutic art of treating bronchitis During the first few days the catarrhal inflammation was treated by revulsive methods dry or wet cups sinapisms At the same time purgatives were given and the patient made to sweat profusely by the application of heat and the administration of diaphoretics Mild antipyretic mixtures usually were added or a sedative cough mixture When the acute symp

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CHRONIC BRONCHITIS

Chronic bronchitis may follow directly upon an attack of acute bronchitis or it may come on after repeated attacks of acute bronchitis each attack becoming more and more protracted or it may develop insidiously without a definite preceding bronchial or pulmonary infection or it may follow exposure to irritating dust and fumes Very frequently it accompanies chronic pulmonary disease of every kind tuberculosis silicosis abscess tumors chronic passive congestion and others The symptoms of chronic bronchitis are of themselves inconvenient annoying and partly incapacitating but its conspicuous importance depends upon the grave complications to which it so often leads chiefly emphysema asthma atelectasis and bronchiectasis

Pathology

The pathology of chronic bronchitis is an extension of the pathology of acute bronchitis In acute bronchitis the inflammatory changes occur chiefly or entirely in the superficial layers of the bronchi in chronic bronchitis they penetrate more deeply and cause profound changes in the bronchial wall The mucous membrane is always of deep red color and on the surface of the bronchi there is more or less mucoid or mucopurulent secretion The bronchi nearly always are somewhat dilated especially the smaller bronchi although saccular or fusiform bronchiectasis rarely is found In some instances the mucous membrane is greatly thickened and indurated it may have a shaggy or villous appearance and the walls of the bronchi are infiltrated and thickened To these changes the term *hypertrophic bronchitis* has been given In other instances the mucous membrane is thin covered with a flat epithelium or completely denuded and the bronchial wall is thin and atrophic To these changes the term *atrophic bronchitis* has been given They do not represent different conditions but different stages of the inflammatory process and may be present side by side in the same lung Nearly always are seen bronchi occluded by tough plugs of mucopurulent secretion which are removed with difficulty

Symptoms

There are only three symptoms of chronic bronchitis namely cough expectoration and shortness of breath The cough is variable at times it may be slight and inconspicuous at other times severe and harassing

toms had subsided an expectorant compound was substituted ipecac tartar emetic squill antimony ammonium chloride potassium iodide senega benzoic acid usually were combined in one form or another to meet the purpose

These methods formerly so highly prized are now almost completely neglected The patient is put to bed in a well aired room but protected from draughts and chilling A laxative often is given Acetyl salicylic acid acetphenetidin pyramidon will relieve headache and general muscular pain Atropine may decrease excessive nasal discharge and diminish swelling of the nasal mucous membranes So called rhinitis tablets are very popular Codein and heroin are satisfactory sedatives when cough is severe and are best given alone as occasion requires Unfortunately heroin no longer is available in the United States

Steam inhalations often are very comforting especially to children Mothers should be warned against instilling oily substances into the noses of infants and young children since there is the real danger of oil pneumonia Almost equally pernicious is the practice of constantly spraying the noses and throats of children with solutions of the silver salts I have seen many instances of argyria acquired in this way

There is no satisfactory method of *preventing bronchitis* What a boon it will be when we are able to protect against the common cold Unfortunately immunity to the common cold is brief and evanescent and we know of no way artificially to establish immunity nor to fortify and extend acquired immunity Efforts have been directed especially towards increasing resistance to secondary invaders Vaccines prepared from the group of bacteria commonly found in infections of the air passages have been used extensively It is impossible to come to a satisfactory conclusion about their value Estimates depend upon impressions I know many patients who would not dare go through a winter without being previously fortified by the injection of vaccines so convinced are they of their beneficent protection I know as many others who have taken them repeatedly without the least benefit

Undoubtedly exposure particularly chilling of the body surface predisposes to bronchitis This belief is firmly rooted and in most languages the name for the common cold is synonymous with cold or exposure How exposure operates is not understood Apparently in some way it lowers resistance and facilitates infection with the virus of common cold or breaks down the barriers to the entry of secondary invaders One method of preventing acute bronchitis is to take sensible precautions against exposure and chilling

lungs thereafter remain quite normal However often the asthma persists into adult life and when it does chronic bronchitis and emphysema gradually develop The patients then always have cough and expectoration with recurring attacks more or less severe of asthma The condition is commonly spoken of as *asthmatic bronchitis* An identical condition may result from a preceding chronic bronchitis It is assumed that these patients become sensitive to the bacteria causing the bronchitis and this hypersensitiveness brings on attacks of asthma Usually they are wheezy very short of breath and the sputum contains numerous eosinophils and Charcot Leyden crystals This condition has been named *bronchitic asthma* Often at a given time it may be difficult to say whether a patient has asthmatic bronchitis or bronchitic asthma Usually a careful consideration of the history of the illness will set straight the sequence of events Sometimes patients with asthmatic bronchitis or bronchitic asthma raise large quantities of thin watery sputum Grossly the sputum resembles the expectoration of pulmonary edema but it is distinguished from it by a low content of albumin This condition has been called *bronchitis pituitosa* and *asthma humidum*

Chronic bronchitis is always present with chronic passive congestion of the lungs For instance in mitral stenosis the early symptoms may be entirely pulmonary cough mucopurulent sputum often bloody shortness of breath a little fever scattered sonorous rales and moist rales at the bases When you recall that it is very easy to miss the signs of mitral stenosis it is not surprising that sometimes mitral stenosis is overlooked and the symptoms accepted as those of some pulmonary disease I have known cases of mitral stenosis to be sent to the tuberculosis sanitarium In older people an intractable bronchitis may be the earliest indeed the only symptom of beginning heart failure The evidence of heart disease may under these circumstances be only vague and indefinite and the true state of affairs be made clear years later when more obvious symptoms of heart failure appear In old people with bronchitis and a degree of emphysema it is often very difficult to decide whether increasing shortness of breath is due to the pulmonary condition or to beginning heart failure Many mistakes are made

A special word should be said about the chronic bronchitis which follows the inhalation of irritant or corrosive fumes and the inhalation of dust The cause of the bronchitis following the inhalation of dust may be due to (1) the irritating effect of the dust upon the bronchial mucous membrane (2) the introduction of bacteria and moulds with the dust and (3) the development of hypersensitiveness to protein particles contained in the dust Many workers in dusty trades develop chronic

Often it is accompanied by wheezing. The sputum is equally variable: at times it consists only of mucoid masses resembling boiled tapioca, at other times of abundant mucopurulent expectoration. There is always shortness of breath on exertion, though usually not pronounced unless emphysema has developed. As a rule the symptoms of chronic bronchitis display a decided seasonal variation. In the summer months they may vanish completely, to recur in the autumn and persist throughout the winter. In later stages they may never entirely disappear but still be aggravated during the winter. Even at a time when symptoms are absent there persists some abnormality in the bronchi which needs but an added mild inspiratory infection to start again a long siege of cough, expectoration and dyspnea.

The diversified clinical manifestations of chronic bronchitis depend upon the pulmonary diseases with which it is associated. When these diseases are apparent the accompanying bronchitis receives little attention and does not deserve the distinction of a place in the diagnosis. However, at times the presence of chronic bronchitis is obvious but the more important disease with which it is associated is hidden and may be overlooked easily. The precision of pulmonary diagnosis has been greatly advanced by roentgenography and bronchoscopy, so much so that these errors are less frequently made than they were formerly. Nevertheless, even now grave pulmonary disease may hide behind the mask of chronic bronchitis, and to avoid deception it is still necessary that we be on our guard.

It has been emphasized again and again that pulmonary tuberculosis is always accompanied by chronic bronchitis. Usually the presence of tuberculosis is discovered easily through the constitutional symptoms, the local pulmonary manifestations and the finding of tubercle bacilli in the sputum. However, in chronic fibroid types of tuberculosis the accompanying bronchitis and emphysema may occupy the center of the stage and the presence of tuberculosis be unsuspected until after diligent search tubercle bacilli are found in the sputum. It is also true that chronic bronchitis may precede the onset of tuberculous infection. This occurs particularly in silicosis, for chronic bronchitis is often the earliest symptom of silicosis. In the old days before the roentgen technic was satisfactorily developed, many cases diagnosed chronic bronchitis frequented the outpatient department of hospitals for years before some enterprising and diligent student finally demonstrated tubercle bacilli in the sputum.

Children hypersensitive to pollens, animal hair or feathers who have attacks of asthma may, as they grow older, stop having attacks and the

lungs thereafter remain quite normal However often the asthma persists into adult life and when it does chronic bronchitis and emphysema gradually develop The patients then always have cough and expectoration with recurring attacks more or less severe of asthma The condition is commonly spoken of as *asthmatic bronchitis* An identical condition may result from a preceding chronic bronchitis It is assumed that these patients become sensitive to the bacteria causing the bronchitis and this hypersensitiveness brings on attacks of asthma Usually they are wheezy very short of breath and the sputum contains numerous eosinophils and Charcot Leyden crystals This condition has been named *bronchitic asthma* Often at a given time it may be difficult to say whether a patient has asthmatic bronchitis or bronchitic asthma Usually a careful consideration of the history of the illness will set straight the sequence of events Sometimes patients with asthmatic bronchitis or bronchitic asthma raise large quantities of thin watery sputum Grossly the sputum resembles the expectoration of pulmonary edema but it is distinguished from it by a low content of albumin This condition has been called *bronchitis pituitosa* and *asthma humidum*

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bronchitis only those exposed to silica or asbestos develop pneumonoconiosis at least to a degree which has clinical significance Many observers think bacteria and moulds carried in with organic dust are the cause of the bronchitis The earliest symptoms of certain fungus infections for example aspergillus may be severe and persisting bronchitis Those who work in organic dust frequently react to early contact with severe constitutional symptoms and bronchial irritation After recovery from these reactions they often go back to work without a return of symptoms although many workers have a chronic cough Those exposed to pulverized grains especially bakers often have chronic bronchitis and many suffer from asthma Irritating fumes are a common cause of chronic bronchitis and when the fumes are corrosive very severe bronchial destruction may occur Recently I saw the lungs of a worker exposed to the fumes of sulphur dioxide who after years of coughing finally died at thirty one years of age of pulmonary carcinoma The bronchial epithelium showed the most extensive metaplasia suggesting that the carcinoma was the result of the changes in the bronchial epithelium induced by the irritation of the sulphur dioxide

Older authors describe *putrid bronchitis* as a particularly virulent form of bronchitis The patients have fever and cough up large amounts of purulent sputum with a fetid odor We now recognize these symptoms as characteristic of a *fuso spirochetal infection* Vincent s infection usually occurs as a secondary invasion especially when as a result of bronchial occlusion or bronchial dilatation pulmonary drainage is blocked Whether or not it ever occurs as a primary and independent infection without preceding injury to the bronchi is questioned although many authors believe that it does It is important to recognize the presence of a fuso spirochetal infection because it can be controlled and often eliminated by the intravenous injection of neoarsphenamine

Complications

The complications of chronic bronchitis are emphysema asthma atalectasis and bronchiectasis In discussing bronchostenosis I pointed out the important part played by bronchitis as a cause of bronchial occlusion Swelling of the bronchial mucous membrane plugs of tenacious mucoid secretion and destruction of the muscular and elastic fibres of the bronchial wall which destroys their power to dilate and shrink to elongate and to shorten with respiration lead to partial or complete obstruction of the lumen and stagnation of secretions Depending upon the size of the bronchi occluded and the degree and du

ration of the obstruction emphysema or atelectasis will result Partial occlusion tends to produce emphysema complete occlusion atelectasis The accompanying infection facilitated by interference with drainage leads to weakening of the bronchial wall and under appropriate conditions of pressure to dilatation of the bronchus

Emphysema regularly accompanies chronic bronchitis of long standing When the emphysema is advanced it causes severe often extreme dyspnea and a readjustment of the respiratory function to meet the reduced pulmonary ventilation All of this is set forth in some detail in the section on emphysema in the discussion in this chapter of symptoms of bronchostenosis and in the discussion of emphysema in the chapter on Diseases of the Lungs (Chapt III Vol II) and there also is described the mechanism by which bronchitis induces emphysema

The relation of bronchitis to asthma has been described already More need not be said it will suffice merely to point out again what a heavy burden the complication of asthma adds to the patient with chronic bronchitis already suffering from cough and dyspnea

In adults bronchitis seldom causes noticeable atelectasis In children especially in infants atalectasis often occurs It is true that it occurs chiefly with acute bronchitis and is often the forerunner of pneumonia In discussing the pathogenesis of bronchiectasis the importance of bronchial obstruction and atelectasis has been emphasized sufficiently In chronic bronchitis of long standing there is nearly always some dilatation of the bronchi often of the terminal ramifications although only rarely do we find saccular or fusiform bronchiectasis Bronchography carried out routinely in patients with chronic bronchitis demonstrates the presence of dilated bronchi in a large proportion of the cases By this method Ochsner examined a large group of students with chronic cough often without expectoration and found bronchial dilatation in about ninety per cent He does not speak of these dilatations as bronchiectasis because he made the unexpected observation that following treatment not only did the symptoms disappear but also the roentgenographic evidence of dilatation Likewise Christopherson on the basis of over 200 examinations concludes that in only a very small percentage of cases of chronic bronchitis do we fail to find some evidence of alteration in the caliber of the bronchial tubes The usual picture is a varicose beaded or fusiform appearance of the bronchial tree most pronounced as a rule in the larger tubes Apparently Christopherson also considers these changes reversible since he regards them as being due to alteration in the autonomic nervous system leading to relaxation of the bronchial musculature Whatever the cause of these bulgings and dilatations may

be there is little doubt that when the conditions producing them are long maintained the alterations in the bronchial lumen become permanent

Diagnosis

Chronic bronchitis produces no characteristic physical signs The diagnosis must be made from the symptoms and the clinical history There may be scattered sonorous and sibilant rales but as in acute bronchitis the lungs may be clear even at a time when there is cough and abundant sputum When physical signs other than rales are present they are the physical signs of complicating disease Of these emphysema is the commonest

The diagnosis of chronic bronchitis is made readily but having decided upon the presence of chronic bronchitis we must then search carefully for associated disease or complicating factors Many physicians urge that every patient with chronic cough should have a bronchoscopic examination and lipiodol roentgenograms It is a wise precaution and will avoid many mistakes Tumors malignant and benign granulomata of the bronchial wall ulcers tuberculous and otherwise bronchial obstruction due to pressure from enlarged lymph nodes or other causes may all produce the symptoms of chronic bronchitis In addition to these bronchial dilatation can be discovered only by bronchography I have already pointed out the importance of considering the possibility of pulmonary tuberculosis and of searching the sputum carefully for tubercle bacilli In older patients evidence of beginning heart failure should be diligently sought

Treatment

The treatment of chronic bronchitis is almost entirely symptomatic yet with care the symptoms may be alleviated and the progress of complications checked The matter of first importance is an appropriate regulation of the patient s habits of living All sources of bronchial irritation should be avoided dusty locations smoke filled rooms etc Smoking should be curtailed and if possible abandoned Exercise must be limited especially if there is dyspnea The patient should sleep in a well ventilated room but it should not be too cold An abundance of rest is necessary Every precaution should be taken to avoid exposure and chilling On very cold or inclement days the patient should remain indoors For those who can afford it a sojourn in a warm climate during the severe winter months is very desirable Acute respiratory

infections are the greatest mishap which can befall a patient with chronic bronchitis In addition to avoiding chilling and exposure to the weather the patient must shun mingling with crowds during the season of prevalent colds and flee from friends infected with colds The diet should be suitably arranged abundant for the lean restricted for the fat Chronic bronchitis is especially common in the obese and the symptoms are often relieved by a gradual loss of weight Alcohol may be used only in moderation the chronic cough of alcoholics is well known

It is common practice to search carefully for localized infection in the upper air passages It is generally thought that infected teeth infected tonsils infected sinuses may constantly reinfect the bronchial tubes I have not seen glowing results from the eradication of such foci of infection and yet I approve of their removal when the presence of infection has been indubitably established Of course we can expect no *more from their removal than the prevention of recurring infection* Nevertheless if this expectation is fulfilled the patient s symptoms may *be ameliorated and the progress of the disease retarded Perhaps the* elimination of upper respiratory infections may play a more fruitful role in prevention than in cure

During exacerbations of the bronchitis the patient should remain in bed until the acute symptoms have subsided Inhalations of steam or remaining constantly in a steam laden room may be helpful certainly it often relieves the cough and allows the sputum to be raised with less effort All manner of aromatic inhalants have been recommended but it is doubtful that they accomplish more than the steam alone

Drugs are of little value The most useful is codein given to control excessive cough It is often prescribed in a mixture with expectorant drugs but I prefer to give it alone so that the dose may be regulated conveniently to suit the indications Potassium iodide is recommended almost universally At times it does seem to act satisfactorily as an expectorant but often accomplishes nothing useful When the secretion is watery and abundant atropine may be helpful If there is reason to conclude that the chronic bronchitis is a symptom of heart failure then the administration of digitalis may bring about spectacular relief When bronchial spasm and asthma occur they must be treated as asthma is usually treated Desensitization with an antigen prepared from the bacterial flora of the patient s sputum may be attempted Sometimes it appears to be beneficial at other times it fails utterly When a fuso spirochetal infection is present these organisms and the fetid odor which accompanies them may be removed by the intravenous injections of arsphenamine or neoarsphenamine

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ysms of coughing are intense the casts being loosened and brought up only with great difficulty These severe symptoms are no doubt due to the fact that the exudation of fibrin is wide spread throughout the bronchial tree Occasionally the casts cannot be dislodged and the patient dies of suffocation The acute form of the disease lasts from one to three weeks

Fortunately the *chronic form* of fibrinous bronchitis occurs much more frequently than the acute form The symptoms are milder due perhaps to the fact that the fibrinous exudate involves smaller areas of the lung at one time There is seldom fever the dyspnea is less intense the cough not so severe The casts usually are smaller and may easily be missed unless the sputum is carefully inspected The expectoration of casts may occur at intervals over a period of many years from one or two to ten or more casts may be brought up daily

There are no *physical signs* characteristic of the condition Usually sonorous and sibilant rales are heard sometimes localized over the area where the casts are forming When other physical signs are present they are due to the associated pulmonary disease or to complications The complications are chiefly bronchostenosis and its results Massive pulmonary collapse sometimes occurs as it did in the case reported by Perlstein

We do not know by what mechanism the fibrinous exudate is pro duced It is certainly not an ordinary result of infection Some authors expres *the view that it is due to a metabolic disturbance or to a faulty* action of the vegetative nervous system likening fibrinous bronchitis to membranous colitis

There is no satisfactory *treatment* for the condition In some cases potassium iodide seems to be helpful in others the inhalation of steam Emetics may assist the dislodgement of obstinate casts For this purpose some physicians recommend forceful compression of the chest during expiration The oxygen tent is a great boon when dyspnea is pronounced In suffocative cases it might be feasible to remove the cast through the bronchoscope although as far as I know this has never been done

Bronchiolitis Fibrosa Obliterans

Bronchiolitis fibrosa obliterans is the name given to an inflammatory reaction in the bronchioles which is followed by scar formation and oblit eration of the lumen of the bronchioles It is not a specific disease but a reaction to the severe damage the bronchioles have sustained It often follows specific infections particularly those usually associated with

Fibrinous Bronchitis

Fibrinous bronchitis is a rare condition characterized by the expectoration of bronchial casts Bettman in 1902 reported a typical case and collected 145 instances from medical literature Bassett wrote a good summary of the condition in 1909 Perlstein in 1930 without giving any particulars states that about 176 cases had been reported up to that date Nothing of importance has been written about the condition since then The fullest and best descriptions of the condition are in the older medical literature

The *casts* usually occur in the sputum as whitish masses which reveal their structure only when gently agitated in a dish of water Then they unravel into casts of the bronchial tree consisting of tubes with a number of branchings or sometimes of a complete reproduction of the bronchial ramifications of a whole lobe or even a whole lung The terminal ramifications may consist of twisted filaments resembling Curschmann spirals The larger portions of the casts form hollow tubes the smaller branches are solid Microscopically the casts consist of parallel bundles of fibres with leucocytes and epithelial cells adherent to their surface At times Charcot Leyden crystals eosinophiles and cholesterin crystals are present The casts consist of varying proportions of fibrin and mucin There is no practical advantage in distinguishing as some authors have done between fibrin and mucin casts

The condition occurs as an independent disease but much more commonly in association with other pulmonary diseases and sometimes with general constitutional disturbances It is found with tuberculosis asthma bronchial compression due to tumor aneurysm enlarged bronchial glands fungus infections chronic passive congestion of heart disease pulmonary edema after the inhalations of steam ammonia and smoke It has been observed in typhoid fever scarlet fever measles small pox rheumatism influenza erysipelas and diphtheria Occasionally it occurs with certain diseases of the skin namely pemphigus impetigo and herpes

The *symptoms* are variable Sometimes there is very little cough or dyspnea the casts coming up easily with hawking At other times there is intense dyspnea and suffocative paroxysms of coughing Patients have choked to death from the casts hanging at the bifurcation of the trachea and occluding both main bronchi Usually there is some fever and at times chills precede the paroxysm Hemoptysis may follow the expectoration of the casts

In *acute cases* the symptoms usually are severe Nearly always there is fever dyspnea is pronounced and there may be deep cyanosis parox

In early stages the inflammation of the bronchiole does not differ from that so frequently seen in cases which do not go on to obliteration of the bronchioles The scarring which obliterates the bronchiole must be a reparative reaction which occurs only when the bronchial wall is deeply involved Or it may be at times a peculiar reaction characterized by abundant exudation with loss of the power of absorption as suggested by Fhrich and McIntosh

In the early stage the microscopical picture shows extensive infiltration of the wall of the bronchiole with desquamation of epithelium and often necrosis Following specific infections the cells infiltrating the walls are mostly mononuclears which soon begin to pour out into the surrounding alveoli The alveolar exudate is rich in fibrin Gradually the wall of the bronchiole may be converted into ragged necrotic tissue At the end of a certain period scar tissue begins to form and the bronchiole is occluded The size of the remaining scar depends upon the amount of surrounding alveolar infiltration which has occurred and has become organized

Symptoms

The characteristic symptoms of obliterating bronchiolitis are fever cough dyspnea and cyanosis The disease often is ushered in by chills Fever is irregular The cough usually is irritative hacking with little expectoration Dyspnea and cyanosis grow increasingly pronounced and may become extreme At times the fever sinks the cough and dyspnea disappear and the patient recovers More often after a temporary respite of a week or two the symptoms return become more and more severe and the patient gradually dies of suffocation

There are no characteristic physical signs of obliterating bronchiolitis The striking feature is that so little is found in the presence of such grave symptoms Usually fine moist rales are heard generally distributed There are no signs of consolidation Sometimes the process is localized to one lung or to a single lobe Under these circumstances rales are restricted to the involved area If the patient recovers small well circumscribed opaque areas may be seen in the roentgenogram resembling healed tubercles

Diagnosis

I have said that anatomically the lesions of obliterating bronchiolitis so closely resemble those of tuberculosis that at first inspection this

respiratory complication measles diphtheria pertussis occasionally lobar pneumonia It may also follow the inhalation of chemical irritants ammonia sulphuric acid hydrochloric acid nitric acid war gases In both groups of cases it is preceded by extensive destruction of the bronchiolar wall In those due to inflammation organization of the exudate begins on about the fourteenth day after onset in those due to irritant and corrosives at an earlier period In animals after the inhalation of phosgene organization begins on the fourth or fifth day after the instillation of alcohol as early as the third day Occasional cases have been observed in which the etiology could not be determined Ehrich and McIntosh have reported three instances occurring as a terminal event in nephritics with uremia In these patients examination of the lungs revealed no evidence of necrosis or destruction of the bronchial walls The lungs were edematous and congested and contained fresh areas of pneumonia Ehrich and McIntosh suggest that these changes are toxic not bacterial and that plugging of the bronchioles with scar tissue formation is not the result of a process of repair but due to organization of exudate which cannot be absorbed They compare the process in the lung with the well known serous membrane inflammations which occur in Bright s disease These serous membrane lesions are sterile and are characterized by extensive exudation and a tendency to rapid organization Obliterating bronchiolitis occurs at all ages and the two sexes are equally affected

Pathology

On section the surface of the lung is studded with grayish white nodules usually miliary in size very tough to the touch The appearance closely resembles that of miliary tuberculosis and this is the preliminary diagnosis nearly always made However if the nodules be inspected carefully through a hand lens they are seen to be irregular in outline with fine white streaks radiating in all directions in this way differing from tubercles which are round and smooth Sometimes the nodules are larger and resemble small scattered foci of pneumonia

The essential features of obliterating bronchiolitis relate it very closely to what has been described by MacCallum and others as interstitial bronchopneumonia which is observed frequently after measles and other infectious diseases and was prevalent at camps during the war in association with the influenza epidemic However obliterating bronchiolitis may not be regarded as a specific disease since an indistinguishable reaction often follows destruction of the bronchiolar walls by chemical agents

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diagnosis is nearly always made by the pathologist It is needless to point out how closely the symptoms resemble those of tuberculosis and this is the clinical diagnosis nearly always made In tuberculosis there is more abundant sputum than in obliterating bronchiolitis and the importance of searching carefully for tubercle bacilli is well understood The roentgenogram helps little in differentiation for the picture of the two diseases is identical Occasionally as Blumgart and MacMahon suggest when the disease affects only a portion of the lungs the fact that the patient is getting better as the lesions in the roentgenogram are spreading speaks against tuberculosis Repeated inspection of the ocular fundi may be rewarded by finding a fresh tubercle which assures the diagnosis of miliary tuberculosis

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BLUMGART H L and MacMAHON H E Bronchiolitis fibrosa obliterans clinical and pathologic study Med Clin North America 1929 XIII 197

third ribs and the entire manubrium were drawn in a caudal direction so that during every inspiration there certainly was a distinct diminution in volume of the apex of each lung The fourth rib was stationary and all the ribs below the fourth had an exaggerated bucket handle movement The subcostal angle was excessively widened during inspiration and the hypochondria flared from the median line to an exaggerated degree There was also an excessive protrusion of the abdominal wall So my impression at the time was that there was an overcompensation of excursion in the lower portions of the lung for the want of normal respiratory excursion at the apices

To confirm the interpretation of movement of the upper ribs and manubrium a number of experiments were carried out on dogs by means of which it was shown that we could reproduce exactly the respiratory movements in this child by cutting away the insertions of the scaleni to the upper ribs In the course of these experiments when the manubrium was fixed by grasping it with the forceps the animal had perfectly normal inspiratory elevation of all the ribs and when the anchorage of the manubrium was loosened the respiratory movements seen in the child were again reproduced It seemed clear from clinical and experimental experience that when the first ribs were not fixed by the scaleni inspiratory excursion which was gained normally by the bucket handle movement of the second third and fourth ribs was lost In fact instead of the lung apices being distended during inspiration they were actually diminished in volume

The real significance of this strange inspiratory excursion did not dawn upon me until a later experience A child two and one half years old was under the care of a surgeon who suspected some obstruction in the upper air passages When the child lay at rest in bed it breathed very comfortably and had a perfectly normal color If the child were engaged in play or cried in fact if there were the slightest call upon the respiratory function beyond the requirements of absolute physical quiet there was exhibited a vicious respiratory excursion The child would develop symptoms of suffocation breathed with very great rapidity and developed a pronounced cyanosis in fact the harder the child endeavored to breathe the worse it breathed the more ineffective attempts at breathing became and the deeper the cyanosis grew Unlike the first child described the manubrium and first ribs were fixed but there was a marked retraction from the second to the sixth rib on both sides The seventh rib remained immobile during inspiration but from the eighth rib down there was a violent excursion Inspiratory protrusion of the abdominal wall was excessive the hypochondria had an exaggerated flaring and there was a veritable seesaw between the upper and the lower thorax Dur

on the integrity of the structure and accessibility of the respiratory units which may be modified by any disease of the respiratory structure Ventilation of any part of the lung will also depend on functional excursion of the overlying ribs and subjacent diaphragm As will be shown in the following discussion not only may pulmonary ventilation be very unequally distributed in the respiratory units through disease of the intrinsic pulmonary tissues and air passages but ventilation may be greatly impaired by disease of the motor organs namely the intercostal muscles diaphragm and scaleni Furthermore the phase of excursion in which ventilation occurs will modify the effectiveness of a given volume of ventilation To procure the optimum ventilation by the inspiration of 600 c c of air demands that the 600 c c of air shall be uniformly distributed throughout the respiratory area Any part of the lung which fails to receive its portion of tidal air will contribute unrespired blood to the aortic stream and in proportion to the amount of unrespired effluent blood which is contributed to the left heart by a portion of lung the other parts of the lung must compensate by superventilation Superventilation of one part of the lung will compensate for carbon dioxide excess contributed to the aortic stream from an unventilated part of the lung but superventilation of one part cannot compensate for the contributed anoxemia which comes from an unventilated area The normal lung is an exquisite tonometer but to insure a tonometric function which will justify an inference that alveolar air is in tonometric equilibrium with effluent blood from the lung demands uniformity in ventilation throughout the lung a normal respiratory membrane and a normal blood flow

The gross subdivisions of the lung usually employed are superior and inferior lobes Anterior and posterior lobes would be an equally good if not better descriptive nomenclature This is from an anatomical basis functionally the denominations anterior and posterior lobes are well justified

Respiratory Movements of the Upper Thorax

The mechanism for ventilation of the anterior or upper lobes is provided by action of the scaleni and intercostal muscles

The function of the scaleni is to anchor the first ribs from which the first intercostal muscles have their origin The scaleni do not elevate the first ribs during normal inspiration The second ribs are elevated by intercostal muscles and so are all the lower ribs elevated by action of the intercostal muscles A case which I reported was that of a child four years old who had complete paralysis of all muscles leading from the head and neck to the thorax Inspiration in the child had a very unusual appearance With each inspiration the first and second and

fourth to the eighth were paretic but over the area from the fourth to the eighth inclusive there was distinct retraction during inspiration This patient had a very small vital lung capacity only 1 100 c c In this case the small capacity could not be accounted for by disease of the lung or circulatory system In addition to paralysis of the intercostals above mentioned there was also demonstrable paresis of the left side of the diaphragm The patient was constantly on the border of an anoxemia amounting to cyanosis Very slight physical effort in fact would bring out cyanosis and air hunger Impairment of the vital capacity was due to paresis of the muscles of respiration but in addition to the paresis of the intercostals and diaphragm we had the factor of regional location of paresis which caused rebreathing between the mid portions of the left lung and the lower part of the left lung These instances of paralysis of the scaleni and paralysis of the upper intercostal muscles and that of the mid intercostals show a striking contrast to the cases in which the paralysis is in the lower intercostals Paralysis of the lower half of the intercostals is very well tolerated because this does not produce rebreathing between the upper and lower lung Patients who have transverse myelitis in the mid-dorsal region have their upper intercostals and diaphragm preserved During inspiration there is no diminution in volume of any portion of the lung and when there is no diminution of any portion of the lung during the inspiratory act there can be no reciprocal rebreathing between any two pulmonary regions When all the intercostals of one side are paralyzed the patient is not cyanotic

A little girl eight years old had hemorrhage into the cervical cord following a fall to the ground from a ladder The child had a complete paralysis of all the intercostals of the left side and complete paralysis of the diaphragm of the left side All the intercostals and the diaphragm of the right side functionated normally If we were to assume there was no ventilation of the left lung then it must follow that all of the blood flowing into the left auricle from the left pulmonary veins must be venous blood Under such conditions we certainly would have had a marked anoxemia and air hunger to compensate for the carbon dioxide contributed to the aortic stream by the unrespired blood from the left lung Now nothing of the kind happened The child lay very tranquilly in bed without the slightest sign of cyanosis Although the respiratory rate was accelerated there was not the least sign of respiratory discomfort During respiration there was no retraction of the left thoracic cage There was no rebreathing between the left and right sides The only way however in which the absence of cyanosis can be explained seems to be to suppose that there must have been a lateral movement of the mediastinum so that during inspiration the movable mediastinum must have been drawn toward the

ing the periods of respiratory distress there was no prolongation of either inspiration or expiration in fact both phases were very much shorter than normal The child breathed as often as sixty times a minute

Physical examination and the X ray both failed to reveal any sign of disease of the contents of the thorax The mediastinum heart and lungs gave perfectly normal shadows However the X ray picture did reveal extensive tuberculosis of the upper six dorsal vertebrae The functional picture of this child was paralysis of the upper six intercostal muscles of both sides I was unable however to demonstrate any sign of disease of the intercostal nerves So far as our clinical observations went we were forced to the conclusion that tuberculosis of the upper six dorsal vertebrae was responsible for paralysis of the upper six intercostal muscles and beyond this nothing of a neurological character was demonstrable The vicious respiratory mechanism in this child caused rebreathing between the upper and lower lungs During inspiration the lung on both sides underlying the upper six ribs was diminished in volume and the same time the lower parts of the lung were distended consequent with the descending currents of air the lower lungs were distended with fresh air and also with alveolar air from the upper lung During expiration the lower portions of the lungs were diminished in size and the upper lungs were enlarged Consequently a part of the air expelled from the lower lungs during expiration was driven into the upper lung so when forced respiratory efforts were made there was reciprocal rebreathing between the upper and lower lung which resulted in suffocative symptoms and extreme cyanosis that gave rise to a suspicion of obstruction of the upper air passages Bronchoscopic examination was made in this case and the larynx and trachea were found to be perfectly normal

The difference between these two cases was simply one of degree of rebreathing In the case of the child who had paralysis of the scaleni there was evidently the same vicious cycle of breathing between the apices and the lower portions of the lung but it was not sufficient to produce cyanosis or suffocative symptoms It was sufficient however to require an exaggerated excursion of the lower lungs to compensate for the rebreathing which did exist The real significance however of exaggerated basal breathing in the first child was not clear until the later experience with the child who had paralysis of the upper six intercostal muscles was studied Isolated paralysis of the scaleni and paralysis of the upper intercostals are rare clinical experiences but they demonstrate the importance of the fixative function of the scaleni and the function of the upper intercostals in procuring normal pulmonary ventilation

Paralysis of the mid costal group of muscles with the lesion confined to one side occurred in a case of syringomyelia The intercostals from the

fourth to the eighth were paretic but *over the area from the fourth to the* eighth inclusive there was distinct retraction during inspiration This patient had a very small vital lung capacity only 1 100 c c In this case *the small capacity could not be accounted for* by disease of the lung or circulatory system In addition to paralysis of the intercostals above mentioned there was also demonstrable paresis of the left side of the diaphragm The patient was constantly on the border of an anoxemia amounting to cyanosis Very slight physical effort in fact would bring out cyanosis and air hunger Impairment of the vital capacity was due to paresis of the muscles of respiration but in addition to the paresis of the intercostals and diaphragm we had the factor of regional location of paresis which *caused rebreathing between the mid portions of the left lung* and the lower part of the left lung These instances of paralysis of the scaleni and paralysis of the upper intercostal muscles and that of the mid intercostals show a striking contrast to the cases in which the paralysis is in the lower intercostals Paralysis of the lower half of the intercostals is very *well tolerated* because this does not produce rebreathing between the upper and lower lung Patients who have transverse myelitis in the mid-dorsal region have their upper intercostals and diaphragm preserved *During inspiration there is no diminution in volume of any portion of the* lung and when there is no diminution of any portion of the lung during the inspiratory act there can be no reciprocal rebreathing between any two pulmonary regions When all the intercostals of one side are paralyzed the patient is not cyanotic

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right side and moved toward the left side during expiration In this wise during inspiration there would be some increase in the transverse diameter of the left lung and a corresponding diminution in the transverse diameter of the right lung but the increase in the longitudinal and anteroposterior diameters would compensate for diminution in the transverse diameter of the right side Consequently *in this child with complete respiratory paralysis of the whole left side* there was some ventilation of the left lung due to lateral movement of the mediastinum

Patients who have transverse lesions of the lower cervical cord so that the scaleni and diaphragm are the only respiratory muscles preserved do not suffer from respiratory distress or give any evidence of anoxemia as they lie at rest in bed When the scaleni and the intercostals are in tact paralysis of the diaphragm is very well tolerated The patients compensate for the want of descent of the diaphragm by increasing the action of their intercostals but there is no rebreathing between the upper and lower lung and patients exhibit no cyanosis It is clear that if any part of a lung is not ventilated by respiratory action and blood flow in the pulmonary vessels through the unventilated portion continues then of course this unventilated lung portion contributes venous blood to the aortic stream A certain amount of unrespired blood may be contributed to the aortic stream without altering the patient s color or his respiratory comfort but this kind of lesion does not give respiratory symptoms com parable with any lesion which will cause rebreathing between two different parts of the lung Any loss of power in the intercostal muscles or the scaleni which will result in a diminution of a part of the lung during inspiration and consequent return to the original size during expiration must of neces sity cause reciprocal rebreathing between two different portions of lung Such a d sturbance in respiration causes very severe symptoms

These considerations show how essential it is that the inspiratory act should be attended with an increment in all the radii of the chest cavity for otherwise we will have either one portion of the blood contributing unrespired blood to the aortic stream or what is still worse there may be reciprocal rebreathing between different lung areas

Respiratory Function of the Accessory Muscles

Increase in the anteroposterior diameter of the thorax in normal in spiration is due solely to the intercostal muscles When the accessory muscles are employed as in cases of asthma and emphysema their func tion is expended in increasing the anteroposterior diameter of the thorax An increment of the anteroposterior diameter of the thorax will ventilate the anterior or upper lobe but will contribute little to ventilation of the posterior or lower lobes of the lungs Let us assume that the patient has

a vital capacity of 5 000 c c of air now let bronchiolar spasm supervene so that his vital capacity will be reduced to 1 000 c c This 1 000 c c of vital capacity under these conditions will increase the volume of the lung from 4 000 to 5 000 This vital capacity of 1 000 c c of air will be procured from an excursion of the lung from the position of 4 000 to 5 000 and is accomplished very largely through employment of the accessory respiratory muscles which lift the thoracic cage and give the bellows like movement to the thorax which ventilates the anterior or upper lobe In other words the asthmatic or emphysematous patient has a sufficient vital capacity to maintain him in respiratory comfort if the tidal air of the vital capacity were equally distributed throughout the entire respiratory area and it seems quite probable that at least one of the reasons why his vital capacity is not adequate to maintain him in comfort is the unequal distribution of the ventilating air

The Transverse Diameter and the Intercostal Function

Inspiratory increase in the transverse diameter is accomplished entirely through the bucket handle movement of the mid portion of the arcs of the ribs This begins in the axillary line at the third rib increases to the fifth rib is about constant from the fifth to the tenth and diminishes from the tenth to the twelfth The bucket handle movement of the ribs contributes to the ventilation of the lower portion of the upper lobe but its chief contribution is to the ventilation of the upper and mid portions of the posterior lobe The longitudinal diameter of the thorax is increased solely through the descent of the diaphragm The excursion of the diaphragm is downward and forward so that the excursion of the anterior abdominal wall is a direct measure of phrenic excursion

Clinical Study of Lung Ventilation

In studying the respiratory excursion of the lung one must observe the ventilation of the upper or anterior lobe and ventilation of the lower or posterior lobe If the scaleni are functioning the manubrium and first ribs will be fixed but the second third fourth and fifth ribs move simultaneously but with different degrees of excursion The excursion of the third rib exceeds that of the second the excursion of the fourth exceeds that of the third and the excursion of the fifth exceeds that of the fourth This is due to the increment of the arcs of the respective ribs and gives an undulatory character to the movement from the second to the fifth ribs inclusively If the ends of the fingers of one hand are placed on the second third fourth and fifth ribs —in a line drawn from the mid clavicular line on the second rib to the anterior axillary line on the fifth rib — the

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increase in the arcs of excursion will be plainly palpable and visible and should there be any impairment in the extensibility of the lung this succession of movement from the second to the fifth rib will be affected Any disease of the bronchi or pulmonary parenchyma or pleura may impair the extensibility of the lung and will be distinctly mirrored in a modified movement of the overlying ribs Instead of the succession of movement which we normally see the ribs may all move the same distance or one or more of the ribs may be immobilized It is true that flexibility of movement of the thorax varies in patients but when there is any disparity in extensibility between the two sides of the lung it can be detected with extreme nicety by this simple method of examination Inasmuch as extensibility is the first attribute of the lungs to be modified in any disease it becomes a very serviceable method of detecting the early stages of pulmonary invasion and is particularly valuable when the invasion is unilateral For instance in the early stages of tuberculosis of the apex of one lung impairment of extensibility may be the only physical sign which we can elicit The percussion note may not be modified and there may be no adventitious signs in fact there may be no physical sign to betray any change in volume or density of the lung and impairment of extensibility will be the only demonstrable evidence of disease For this reason routine examination of the extensibility will be the only demonstrable evidence of disease and is of very great clinical service

Respiratory Movements of the Lower Thorax

The respiratory movements of the lower thorax have been a source of much physiological and clinical discussion since the time of Galen Excursion of the anterior abdominal wall has always been clearly ascribable to descent of the diaphragm The lateral movement of the ribs in the mid portions of the costal arc is clearly due to the function of the inter costal muscles but the inspiratory movement of the costal margins or collected ends of the ribs from the sixth to the twelfth has been a source of much debate Finally the question seemed to have been definitely settled by Duchenne (Recherches Electro Physiologiques et Therapeutiques sur la Diaphragme 1853) and Duchenne s interpretation has been accepted by all writers on clinical and physiological subjects

Duchenne found that during inspiration the subcostal angle widened and the costal margins moved away from the median line when the inter costal muscles were paralyzed and only the diaphragm was functionating

He found also in experiments on dogs that when the viscera of the upper abdomen were removed there was an inspiratory narrowing of the subcostal angle and the entire costal margin moved toward the median line His interpretation was that on account of increase in intra abdominal pressure due to descent of the diaphragm the hypochondria were pushed in an outward direction and thus gave rise to inspiratory widening of the subcostal angle but when the liver spleen and stomach were removed so that the viscera were not driven downward during the descent of the diaphragm then the insertions of the diaphragm to the ends of the ribs caused narrowing of the subcostal angle and the costal margins in their entire extent were drawn toward the median line The whole difficulty of the problem lay in the fact that students of the problem before and since the time of Duchenne have failed to differentiate between evidence of excursion of the diaphragm and evidence of activation of the diaphragm In all the works on anatomy and physiology we find Duchenne s interpretation accepted as final and in all neurological works and monographs on the diaphragm the symptoms of diaphragmatic paralysis are very unsatisfactorily discussed

The direction of movement of the costal margins has nothing to do with excursion of the diaphragm The most obvious thing is really the truth the outward movement of the costal margin is due to action of the intercostal muscles and movement of the costal borders toward the median line is ascribable to activation and not to excursion of the diaphragm

The direction which the costal margins will take during inspiration will be the resultant of the conflict between the two groups of muscles—namely the intercostals and the diaphragm If the diaphragm gains mastery of any part of the costal margin then it will move toward the median line during inspiration If the intercostal muscles gain the mastery of the costal margin it will move away from the median line during inspiration In a normal human subject there is a very nice balance in favor of the intercostals so that we see under normal conditions the costal margins move laterally during inspiration

The question which has been raised has been why do the intercostals enjoy the balance of power so far as the movement of the costal margin is concerned The dome of the diaphragm varies greatly in the arc of convexity in its different portions for instance the anteromedian or subcardial portion of the diaphragm has very much less convexity than the lateral or posterior portions of the diaphragm The resultant line of traction from an activated fiber of the diaphragm will be a straight line drawn between the central tendon the point of its origin and the rib the point of its insertion Now it is clear that the more nearly the fibers of the diaphragm coincide with a straight line the more effective will be their

traction on the ends of the ribs during activation And another point of importance in this relation must be mentioned that it requires much less depression of the subcardial portions of the diaphragm than of the lateral and posterior portions to gain the mastery of the costal margins where their respective fibers are inserted and also it must be remembered that different lesions will modify the convexity of the diaphragm in very different ways Emphysema of both lungs will cause flattening of the entire phrenic dome Unilateral pleurisy with effusion and pneumothorax will diminish convexity of one half of the diaphragm Pericarditis with effusion will flatten the entire subcardial diaphragm and leave the lateral and posterior portions unmodified Enlargement of the left ventricle will depress the subcardial portion of the diaphragm to the left of the median line much more than to the right of the median line Dilatation of the right ventricle and right auricle will depress the subcardial diaphragm to the right of the median line much more than to the left of the median line Convexity of the entire diaphragm may be increased by ascites or tympanites the right half of the diaphragm may have its convexity increased by enlargement of the liver while the left half may have its convexity increased by tumors of the spleen or stomach Subphrenic abscess may also increase the convexity of either side In obsolete pleurisy there may be a shortening of the longitudinal diameter of the thorax and an increase in the concavity of the under surface of the diaphragm But in these cases there are always synechia between the diaphragm and the chest wall and consequently the diaphragm is given a new point of insertion instead of being at the end of the ribs it will be at the inner surface of the chest wall So although the under surface of the diaphragm may have its concavity increased there is lessened convexity of the upper surface of the effective portion of the diaphragm

The conformation of the diaphragm will determine the direction of movement of the costal margins consequently the movement of the costal margin gives us some indication of the conformation of the diaphragm This is always an important point in physical diagnosis By direct inspection we determine the conformation of the thoracic cage but it is only by inferential procedures that we can gain any conception of the inferior boundary of the thorax and we cannot pretend to have made a complete physical examination of the chest without forming some conception of the conformation of its inferior boundary and this its most movable boundary

Unlike other skeletal muscles the diaphragm s function does not consist in approximating its origin and insertion but in shortening the line of its arc The resultant of a line of traction is a straight line so the more

nearly the line of the phrenic fibers coincides with a straight line the more effective will be its traction on the costal margin There is some inspiratory advantage in the fact that the intercostal muscles dominate the control of the costal margins Spreading the hypochondria contributes to flattening of the diaphragm during inspiration so that in reality whatever significance the spreading of the hypochondria may have in contributing to inspiration this contribution is made by the intercostal muscles and not by the diaphragm If a young vigorous person be asked to protrude the abdomen or in common parlance to "poke out his stomach" he will strongly contract his diaphragm and then if he is instructed to hold his abdomen in this position and make a forced inspiration it will be seen that during the inspiration which follows the costal margins will be drawn toward the median line although the second phase of excursion is performed entirely by the intercostal margins and is not shared in at all by the diaphragm because the diaphragm has already made its maximum descent before the intercostals are employed During the second phase of this prescribed procedure the diaphragm is activated but does not perform any excursion However the diaphragm is sufficiently flattened by the initial procedure to gain mastery of the costal margin and during the second phase by its further activation it will draw both costal margins toward the median line This is a very simple method of confirming the significance of the flattening of the diaphragm in gaining mastery of the costal margin

Movement of Costal Margins in Clinical Conditions

When the dome of the liver is enlarged by acute changes in the liver as in granular degeneration or in acute diseases of the hepatic parenchyma the right costal margin will be seen to move more promptly and farther in an outward direction than the left costal margin during inspiration In other words if the arch of the right diaphragm is increased the balance of the power is given still further than normally to the intercostal muscles and consequently the outward movement of the costal muscles will be accentuated during inspiration

Subphrenic Abscess—In cases of subphrenic abscess this phenomenon is of particular value The difficulty in diagnosis of subphrenic abscess lies in differentiation from thoracic empyema In both we have dullness at the base of the thorax laterally and posteriorly a loss of tactile fremitus and should there be sufficient synechia between the visceral and parietal pleura so that the lung cannot recede from the pleural sinus as the diaphragm is pushed upward then we shall have bronchial breathing and whispered pectoriloquy so that inspection percussion and auscultation in both subphrenic abscess and thoracic empyema may give exactly the

same results However in the case of thoracic empyema either the outward movement of the costal margin will be diminished or the inspiratory movement of the costal margin will be toward the median line, whereas in four cases of subphrenic abscess which have come under my observation the costal margin on the right side moved farther and more actively away from the median line than did the left costal margin on which side in each case the lung and pleura were unaffected

Obsolete Pleurisy—In cases of obsolete pleurisy with synechia between the phrenic pleura and parietal pleura the arch of the diaphragm is of course accentuated but the effective portion of the diaphragm so far as the movement of the hypochondria is concerned will be that portion of the diaphragm between the central tendon and the point of fixation to the thoracic wall This gives a new point of fixation to the diaphragm The attachment to the costal border has no longer any significance, so far as phrenic excursion or phrenic traction is concerned Consequently the movement of the costal margin will either be restrained or be drawn toward the median line by virtue of the thoracic insertion of the diaphragm which converts its effective part into a plane This can be very easily shown in an animal by suturing the diaphragm to the eighth ribs in the axillary line Immediately this is done the costal margin will be seen to move toward the median line during inspiration and when the suture is released the costal margin will again resume the outward movement during inspiration

Cardiac Enlargement—This portion of the diaphragm has a more flattened arch than the lateral and posterior portion and therefore much less depression of this portion of the diaphragm is required to modify the movement of the costal margin than is required in the case of the lateral and posterior portion of the diaphragm to modify the movement of the costal margin where their fibers are inserted If a patient has an elongated and enlarged left ventricle and the right ventricle and right auricle are not enlarged we may see asymmetry in the movement of the subcostal angle From the subcostal angle to the eighth costal cartilage on the left side there will be a restraint of the border and in some instances the costal margin will move toward the median line during inspiration whereas the right costal margin will move outward When the enlargement of the heart is globular as in synechia cordis syphilitic myocarditis and diseases of the mitral valve we commonly see narrowing of the subcostal angle during inspiration and the inspiratory narrowing may be symmetrical although on both sides below and external to the eighth costal cartilage the borders will move outward during inspiration This observation will frequently save one from the error of underestimating the size of a heart when the person is lying down If the anteroposterior diameter of the thorax is

sufficiently large and the heart mobile the precordial area of dullness may not be enlarged but if under such circumstances there is narrowing of the subcostal angle one may be quite sure there is flattening of the subcardial diaphragm both to the right and left of the median line The enlargement of the precordial area may be confirmed by percussion of the patient in the upright position and by the use of the fluoroscope

Phosgene Poisoning —In the acute stage of phosgene poisoning dilatation of the right ventricle and right auricle is of frequent occurrence The left ventricle and left auricle never dilate during this period In acute pulmonary emphysema which is frequently met with at this time percussion of the right auricle to the right of the sternum is very uncertain or very difficult Flattening of the subcardial diaphragm to the right of the median line however could be recognized by the fact that the right costal margin between the angle and the eighth rib was restrained in its outward movement or it moved toward the median line during inspiration When these patients were given as much as 1 25 of a grain (2 5 mgm) of digitalin subcutaneously and the right heart regained its normal size the costal angle was seen to widen symmetrically during inspiration

Pericarditis with Effusion —Free fluid in the pericardial sac will cause a marked depression of the subcardial diaphragm in fact there is no intrathoracic disease which will cause greater downward displacement of the liver than pericarditis with effusion If the fluid within the pericardial sac is not walled off and lies perfectly free a considerable amount of fluid or fluid in sufficient quantities to impede the diastole of the heart will always give a symmetrical narrowing of the subcostal angle during inspiration and as the fluid is withdrawn we see the inspiratory narrowing converted into inspiratory widening of the costal angle This is the phenomenon which has given rise to an error in diagnosis of paralysis of the diaphragm in pericarditis with effusion The subcardial portion of the diaphragm with large effusion will of course not descend during inspiration but the subcardial portion of the diaphragm is nevertheless activated and gives rise to the narrowing of the subcostal angle

Emphysema —Emphysema due to bronchitis atrophic emphysema emphysema from bronchiolar spasm and acute emphysema from laryngeal stenosis may all cause sufficient flattening of the diaphragm so that the entire costal margin on both sides will be drawn toward the median line during inspiration It is a common experience in chronic bronchitis with emphysema to find the lower borders of the lung sufficiently enlarged to fill the pleural sinuses This will be true during periods of comparative comfort when the patient is not suffering any respiratory distress and there is no cyanosis There may be a period of bronchiolar spasm or an increase

same results However in the case of thoracic empyema either the outward movement of the costal margin will be diminished or the inspiratory movement of the costal margin will be toward the median line whereas in four cases of subphrenic abscess which have come under my observation the costal margin on the right side moved farther and more actively away from the median line than did the left costal margin on which side in each case the lung and pleura were unaffected

Obsolete Pleurisy—In cases of obsolete pleurisy with synechia between the phrenic pleura and parietal pleura the arch of the diaphragm is of course accentuated but the effective portion of the diaphragm so far as the movement of the hypochondria is concerned will be that portion of the diaphragm between the central tendon and the point of fixation to the thoracic wall This gives a new point of fixation to the diaphragm The attachment to the costal border has no longer any significance so far as phrenic excursion or phrenic traction is concerned Consequently the movement of the costal margin will either be restrained or be drawn toward the median line by virtue of the thoracic insertion of the diaphragm which converts its effective part into a plane This can be very easily shown in an animal by suturing the diaphragm to the eighth ribs in the axillary line Immediately this is done the costal margin will be seen to move toward the median line during inspiration and when the suture is released the costal margin will again resume the outward movement during inspiration

Cardiac Enlargement—This portion of the diaphragm has a more flattened arch than the lateral and posterior portion and therefore much less depression of this portion of the diaphragm is required to modify the movement of the costal margin than is required in the case of the lateral and posterior portion of the diaphragm to modify the movement of the costal margin where their fibers are inserted If a patient has an elongated and enlarged left ventricle and the right ventricle and right auricle are not enlarged we may see asymmetry in the movement of the subcostal angle From the subcostal angle to the eighth costal cartilage on the left side there will be a restraint of the border and in some instances the costal margin will move toward the median line during inspiration whereas the right costal margin will move outward When the enlargement of the heart is globular as in synechia cordis syphilitic myocarditis and diseases of the mitral valve we commonly see narrowing of the subcostal angle during inspiration and the inspiratory narrowing may be symmetrical although on both sides below and external to the eighth costal cartilage the borders will move outward during inspiration This observation will frequently save one from the error of underestimating the size of a heart when the person is lying down If the anteroposterior diameter of the thorax is

dealing with a cardiac source of air hunger and not with a pulmonary source of air hunger

Movements of the Diaphragm

Duchenne very clearly states that when dogs have paralysis of all their intercostals and the diaphragm is alone active the costal margins spread during inspiration This is not true in human beings In every case of paralysis of the intercostals which has come under my observation when the diaphragm was still active the costal margins were drawn *toward the median line during inspiration*

In 1913 I made a series of observations on dogs relative to the function of the diaphragm and the intercostals and I always found the behavior of the costal margins in paralysis of the intercostals and paralysis of the diaphragm was exactly the same as I had observed in human subjects In all of these experiments the abdomen was opened so that a clear view of the under surface of the diaphragm could be procured A few years ago I repeated my observations and made sections of the lower cervical cord of a dog without opening the abdomen I was surprised to find the costal margin spread just as Duchenne described but the spread of the hypochondria was not of the same character and not carried out with the same vigor as is seen when the intercostal muscles are active It was clearly a passive spread and not an active widening of the hypochondria An incision was made in the median line so that the abdominal cavity freely communicated with the outside air It was then seen that the entire costal *margin on both sides was drawn toward the median line during inspiration* When the incision was closed by clamps the passive spreading of the hypochondria was again apparent

As it happened the first experiment was done on a setter dog the type of dog which has a long thoracic cage and a very high arch to the diaphragm When the abdomen of this dog was closed and the diaphragm activated there were two forces at play on the hypochondria One was the traction on the costal margins from the diaphragm and the other was increased pressure in the abdominal cavity which accompanied descent of the diaphragm The setter dog has such a high arch to his diaphragm that increase in abdominal pressure exceeded the traction on the costal margin When however the abdomen was opened so that descent of the diaphragm did not increase the intra abdominal pressure then traction of the diaphragm on the costal margins became apparent and both margins in their entire extent were drawn toward the median line during inspiration

Another type of dog was then employed the bulldog which has a shorter thorax and a flatter diaphragm much more like the human diaphragm than that of the setter When the intercostal muscles were

in the severity of the bronchitis. The patient will then have cyanosis and suffer from air hunger and dyspnea. So far as percussion is concerned the conditions remain the same in the periods of acute discomfort and in the interims of euphoria. However, if one will observe the costal margins during the periods of cyanosis and dyspnea the costal margins will be seen to move toward the median line during inspiration. This is the only physical sign which will clearly indicate an increase of volume of the entire lung during the acute attacks. The emphysema of the edges of the lung, though they may fill the pleural sinuses, will not flatten the arch sufficiently to give the diaphragm mastery over the costal borders during inspiration. However, when the great volume of lung is enlarged and the entire leaf of the diaphragm is flattened, then the diaphragm gains mastery of the entire costal margin. This point is of very considerable service in differentiating between genuine bronchiolar asthma and pseudo asthma, both of which frequently occur in the course of chronic bronchitis with emphysema. These patients acquire such a phobia toward their attacks that pseudo asthma becomes a very common experience. The patients cannot differentiate between the pseudo asthma and the asthma due to bronchiolar spasm. The pleural sinus is always filled with emphysematous lung, so that percussion is of no service in differentiating between the genuine and spurious attacks. The true attacks of bronchiolar spasm are always accompanied by inspiratory retraction of the costal margins, and the behavior of the costal margins during false attacks remains just the same as during the periods of comparative comfort. I have on several occasions been able to confirm this observation by relieving the genuine attacks with hypodermic injections of adrenalin, whereas the pseudo attacks were relieved equally well by hypodermic injections of adrenalin or water.

Emphysema Associated with Cardiac Disease.—Chronic bronchitis and emphysema associated with cardiac disease may often give rise to much difficulty in estimating the share which may be played by the cardiac disease and the share which is played by the emphysema. If the patient has cyanosis and air hunger, and inspiratory narrowing of the costal borders is seen throughout the entire costal margin, then we may be sure that the entire diaphragm is flattened, and thus the inference is justified that the total volume of both lungs is greatly increased. If, however, inspiratory narrowing of the subcostal angle and retraction of the costal borders is confined to that portion of the costal margin between the angle and the eighth rib, we know that only the subcardial portion of the diaphragm and not the entire diaphragm is flattened, and if the right diaphragm is not flattened, then the patient cannot have emphysema as a source of his cyanosis. When the costal margins to the eighth rib are involved, we are

costal and intercostal spaces thus both the ribs and the intercostal spaces are seen to be retracted over the pleural sinus In the beginning of the inspiratory movement this initial band of retraction is due to activation of the diaphragm which precedes excursion As excursion of the diaphragm proceeds the band of retraction is erased by a descending shadow which marks the descent of the lower border of the lung into the pleural sinus as the diaphragm is withdrawn from the thoracic wall So that we may speak of the band of retraction in Litten s phenomenon as due to activation of the diaphragm and erasure of the band of retraction as due to excursion of the diaphragm If we are to sum up the visible evidence of activation of the diaphragm under normal conditions Litten s band of retraction is the only visible evidence Evidences of activation of the diaphragm so far as the costal margin is concerned become apparent only with flattening of the phrenic arch Visible evidences of excursion of the diaphragm are the erasure of the band of retraction as described by Litten and protrusion of the anterior abdominal wall

The direction of movement and symmetry or asymmetry of movement of the costal margins are very considerable aids in estimating the following conditions (1) conformation of the heart (2) the size of the pericardial sac (3) the volume of the lung (4) differentiation between pleurisy and pneumonia (5) obsolete pleurisy (6) enlargement of the liver (7) subphrenic abscess (8) pneumothorax (9) paresis of intercostal muscles and diaphragm

It must not be understood that the direction of movement of the costal margins is diagnostic or pathognomonic of any of the above mentioned diseases The movement of the costal margin simply gives us evidence of the conformation of the vault of the diaphragm One may have pleurisy with effusion or a hemothorax without flattening of the diaphragm and in fact there may be a slight pneumothorax without demonstrable phrenic flattening and there may be great enlargement of the heart with little or no depression of the subcardial portion of the diaphragm if there should be an accompanying ascites or any other intra abdominal lesion which would prevent descent of the diaphragm The practical diagnostic point is simply this in making a physical examination we must not merely study the excursion of all the ribs but we must consider the symmetry or asymmetry of excursion of the costal margins and the direction and degree in which they move and we must also study the movement of the upper and internal portion of the costal margin as compared with that of the lower and external margin of the same side When the excursions of the costal margins are *studied in this manner it will often lead to suggestion of pathological* lesions which otherwise would not be suspected and it will often

paralyzed by transsection of the cervical cord the costal margins were drawn toward the median line when the abdomen was unopened The bulldog s diaphragm much like the human diaphragm is sufficiently flat so that traction on the costal margin will overcome the increased lateral pressure produced by descent of the diaphragm

Duchenne and his contemporaries who did the same experiment do not describe the type of dog used but from their conflicting results it is very probable in the light of my own experiments that Duchenne used the setter type of dog and some of his contemporaries who got other results evidently used a bulldog type

There are other clinical experiences which clearly refute Duchenne s interpretation of diaphragmatic phenomena I have observed three cases of large empyema in the left pleural cavity in all of which the spleen was displaced below the costal margin The percussion note was flat from the clavicle to the costal margin and much to my surprise in the first of these patients the costal margin on the affected side moved away from the median line during inspiration although not so far as the right costal margin The idea then occurred that the diaphragm was convex on its under surface and for this reason lost control of the costal margin Two pints of pus were withdrawn from the pleural cavity with a Potain aspirator Then the costal margin was seen to move strongly toward the median line during inspiration The diaphragm was sufficiently elevated to gain control of the costal margin Then three pints more of pus were aspirated and the costal margin again moved away from the median line during inspiration Thus the diaphragm became sufficiently elevated so that it lost control of the costal margin We have here a very excellent proof that the determining factor in the movement of the costal margin does not lie in elevation or depression of the diaphragm but in its convexity and flattening and it is quite the same whether it is convex on the under surface or on the upper surface In both cases it will lose control of the costal margin

In a recent case of pressure hydropneumothorax of the right side with the fluoroscope we could clearly see the concavity of the upper surface of the diaphragm and the diaphragm could be clearly seen to rise during inspiration The right costal margin moved away from the median line although the liver was of course seen to rise instead of descend during inspiration When air was released from the pleural cavity so that barometric pressure prevailed in the pleural cavity the costal margin was drawn toward the median line during inspiration

The Litten Diaphragm Phenomenon

The diaphragm phenomenon described by Litten consists of a visible band of retraction which occupies the pleural sinus and includes both

muscular power or because the phrenic arch has been elevated and the disparity between the curve of the effective muscle fibers and line of traction has been increased

Should the costal margin of one side show lessened movement but in an outward direction then there may be (1) partial loss of domination of the costal margin by the intercostals due to moderate flattening of the phrenic arch (2) any lesion which will impair extensibility of the lower part of the lung and thus retard excursion of the ribs (3) restraint of the costal margins due to spasm of the abdominal muscles

Excursion of the costal borders can be studied only when the patient is lying down with all abdominal muscles relaxed In the upright position the abdominal muscles restrain the outward movement of the costal margins The borders should be carefully palpated in their entire extent and movement related to the median line must be carefully differentiated from movement anteriorly and upward It is only movement laterally and toward the median line which concerns the balance between the diaphragm and intercostal muscles

This method of studying thoracic excursion has been of very great diagnostic aid and has greatly enhanced the interest in cardiorespiratory as well as nervous diseases and diseases of the upper abdomen

give us information on the contour of the diaphragm which is otherwise quite neglected This method of studying the diaphragm gives us information which even the X ray and fluoroscope fail to give for the X ray simply gives us a silhouette of the projected dome of the diaphragm and does not give us accurate information on the curvature and function of different parts

Hernia of the Diaphragm

Hernia does not modify the movement of the costal margin or protrusion of the anterior abdominal wall during inspiration

Recently a man with a large hernia of the stomach through the left diaphragm which the patient had carried for many years presented the following objective signs the volumes of the two sides of the thorax were symmetrical over the left base and infrascapular and lower axillary region there were distinct dullness diminution in tactile fremitus and elevation in the pitch of the respiratory sounds an intrathoracic succussion was clearly demonstrable there was no coin sound In spite of these signs however it was observed that the costal margin on the left side retained a perfectly symmetrical movement with the costal margin of the right side This fact alone gave rise to suspicion of a hernia of the diaphragm In fact I can conceive of no other condition which would give the described intrathoracic signs and not modify the movement of the costal margin The diagnosis was easily confirmed by giving the patient a barium meal which was swallowed under observation with the fluoroscope

Summary

Routine examination of patients should include careful observations on the manner of movement of the costal margins The direction in which that part of the costal margin may move which lies between the subcostal angle and the eighth rib should be studied in comparison with the movement of the lower and outer portion of the costal margins and the symmetry or asymmetry of movement of the two borders in their inner and outer portions should be determined

Should any part or all of both costal margins move toward the median line during inspiration then the diaphragm attached has gained mastery over the opposing intercostal muscles because (1) the involved diaphragm is flattened (2) the opposing intercostal muscles are paretic (3) there are synechiae between the diaphragm and the inner surface of the chest wall thus giving a new insertion of the diaphragm Should the costal margin of the affected side move farther outward than the costal margin of the normal side then traction on the costal border from activation of the diaphragm has been lessened either because of an impairment of

CHAPTER III

DISEASES OF THE LUNGS

By SIDNEY J SHIPMAN

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INTRODUCTION

In recent years significant advances have been made in our knowledge of diseases of the chest For the most part these have resulted from the more precise employment of old tools The revolutionary changes however such as those brought about by the induction of specific microbial agents have played a dramatic part in progress, and the recent advances in the knowledge of human respiratory physiology have been of inestimable value in clarifying our knowledge of diseases of the chest We have a more exact understanding of pulmonary ventilation the distribution of gases over alveolar surfaces the diffusion of gas through the alveolar capillary membrane and the mechanism of the pulmonary circulation are much better understood The study of the relationship of these conditions to other conditions and their relation to each other has led to much greater accuracy in diagnosis Cardiac catheterization has been of great help Our knowledge of cor pulmonale has been clarified Pulmonary insufficiency can now be recognized early in its inception and its course more adequately treated Bronchospirometry although it must be employed by expert hands has been of enormous value in permitting the study of the function of the two lungs separately and has proved to be especially useful before radical surgery is under taken The relation of anoxemia to cyanosis has been clarified This is important since one of the early signs of pulmonary insufficiency is anoxemia Because of its simplicity the oximeter can be employed in clinical practice to aid in attaining a better understanding of alterations in physiology The proper appreciation of the fact that a red blood cell is exposed to fresh oxygen for not longer than one tenth of a second underlines the importance of intake respiratory function in avoiding the effects of anoxemia More accurate studies have re-

emphasized the importance of ciliated mucosa of the respiratory passages in the protection of the lung against bacteria and foreign matter This has an important clinical application in the use of aerosols especially those that paralyze the cilia as in the use of too concentrated solutions of epinephrine

Precise anatomical studies have elucidated the bronchopulmonary segments As a consequence in patients with pneumonia and atelectasis the exact location of tumors may be more accurately determined even though they are beyond the reach of bronchoscopic vision Chest surgeons have been immeasurably aided by these studies Surgical advances following in the wake of modern anesthesia have been of great value in restoring physiological efficiency as in the operation of decortication and the obliteration of pleural dead spaces

Important advances have been made in the study of the mycoses especially coccidioidomycosis and histoplasmosis The relative frequency of the former in California and Arizona and of the latter in the Mississippi Valley Basin has clarified many of the puzzling factors of intrapulmonary diseases in these areas

The vogue of inhaling metallic aluminum in the hope of alleviating the effects of silicosis has come and gone Beryllosis has found its place as a serious and fatal pulmonary manifestation

Significant advances have been made in our knowledge of carcinoma of the lung Tobacco smoking as an etiological factor has been emphasized and while opinion has not yet crystallized there is convincing evidence that it plays some part in the origin of this disease Bronchial adenomas especially in women have been more commonly recognized and the assumption that they are always benign has been seriously questioned

The cytological examination of sputum for exfoliated cancer cells is a development of great importance and it seems likely that it will be used with increasing frequency in the years to come

DISEASES DUE TO CIRCULATORY CHANGES

Pulmonary Congestion

It is customary to distinguish between active and passive congestion of the lungs Active congestion is an important element in the reaction of inflammation but does not occur apart from the other components of

this reaction Passive congestion is due to obstruction of the flow of blood from the lungs to the heart It is merely one of the many symptoms caused by the condition producing the obstruction However, whereas active congestion cannot be separately distinguished from the other manifestations of inflammation passive congestion produces a characteristic group of symptoms which gives it an independent clinical position

Active Congestion

Active congestion or hyperemia is associated with every inflammatory disease of the lungs and scarcely deserves any separate mention The most striking type of hyperemia is the stage of engorgement in lobar pneumonia French authors have described under the name of Woillez s disease a form of pulmonary congestion characterized by a short period of fever cough and sputum a little impairment of the percussion note diminished or slightly blowing breath sounds and fine moist *rales* The symptoms are mild and end in recovery Cultures from the sputa and lung puncture material have demonstrated in nearly all instances the pneumococcus that is supposed from animal experiments to be an attenuated form of pneumococcus These cases have all the characteristics of a mild or abortive pneumonia and should properly be considered under that heading In some of the acute specific infections frequently complicated by pneumonia death may occur while the lungs are intensely congested and before much exudation has occurred a condition to which the name hemorrhagic pneumonitis' has been given

Passive Congestion

Passive congestion is always the result of obstruction to the blood flow in the pulmonary circulation The most common cause is disease of the mitral valves but it occurs frequently in aortic insufficiency in myocardial disease and in myocardial insufficiency from whatever cause In passive congestion the lungs feel tough and resistant and the cut surface is red The capillaries are engorged and distended and project as loops into the alveolar spaces The term red induration has been applied to this condition If the congestion lasts for a long time

the lungs become thickened and indurated owing to the growth of connective tissue in the alveolar walls and they acquire a brown color from the deposition of pigments derived from the hemoglobin of destroyed red blood corpuscles This condition is described as brown induration The alveoli contain degenerated epithelial cells red blood corpuscles a few leucocytes and large round cells filled with brown pigment granules the cells commonly called heart failure cells There is a varying amount of serous fluid in the alveoli The bronchial walls are congested and the mucous membranes often a little swollen

The *symptoms* of chronic passive congestion are dyspnea cough and sputum

Dyspnea Passive congestion has a profound effect upon pulmonary ventilation Unfortunately we rarely have an opportunity to study the effect of passive congestion alone because it is nearly always secondary to heart disease Observations made upon the respiration of cardiac patients however and of animals in whom passive congestion has been produced experimentally clearly demonstrate that the pulmonary congestion plays an important role in the development of dyspnea Daily clinical experience teaches us that dyspnea and cyanosis are particularly prominent symptoms in patients with heart disease that is accompanied by pulmonary congestion For example in mitral stenosis dyspnea comes on very early in the disease in aortic insufficiency at a similar stage it is conspicuously absent and it never becomes prominent until relative mitral insufficiency has developed The best way to test the degree of dyspnea in cardiac patients is to measure the vital capacity of the lungs that is the volume of the greatest possible expiration after the fullest inspiration The vital capacity of the lungs varies proportionately with the degree of dyspnea and is an accurate index of the respiratory capacity of the patient When the patient is resting comfortably in bed a diminution of vital capacity without any other appreciable change in his condition presages the onset of dyspnea The mechanism of dyspnea in heart disease is precisely the same as in health for in both circumstances an increased respiratory demand is met by an increased ventilation of the lungs The essential difference is in the range of functional accommodation In health the respiratory capacity may be increased up to eight times the normal whereas in heart disease pulmonary ventilation can be augmented only a little This loss of ability to increase adequately the depth of respiration may be accounted for in two ways Since the lungs are confined within a rigid chest as they become more and more engorged with blood they can accommodate less and less air

The distended capillaries may actually be seen protruding into the alveoli and diminishing their lumen The dilated vessels also reduce the resiliency of the lungs and if the congestion lasts a long time fibrous tissue grows in the alveolar walls and further impairs the elasticity Which of these two factors is the more important it is impossible to say, but probably in the early stages of congestion the space filling effect of the engorged blood predominates and at later stages the rigidity of the lungs plays an increasingly important role

Cough varies with the intensity of the congestion and the degree of bronchial inflammation With congestion of long standing bronchitis is always associated and it not only causes cough often of a most harassing character but if severe it further complicates the situation by causing pulmonary distention

The *sputum* varies in amount and character The associated bronchitis gives it a mucopurulent character but it is richer in albumin than the sputum of simple bronchitis because of the admixture of serous exudate from the alveoli The sputum often contains streaks or flecks of bright blood but is more commonly of a yellowish-red tone with spots of deeper rusty brown color This coloring is given by the iron containing pigments of altered hemoglobin Microscopical examination discloses the characteristic heart failure cells

The *physical examination* of the lungs shows little change in percussion The pulmonary distention may give an increased resistence to percussion and a hyperresonant quality to the note The pulmonary excursion is limited The breath sounds often are diminished in intensity especially over the lower lobes or they may be harsh and roughened Fine moist *rales* are heard over the bases and frequently sonorous and sibilant *rales* are generally distributed

The *roentgenogram* is often distinctive The hylus shadows are deepened and widened the lung fields cast a deeper shadow than normally and the shadow of the ramifications of the bronchial tree is very wide and deep These shadows are cast by the distended pulmonary vessels and lymphatics

The *diagnosis* of pulmonary congestion is difficult before the onset of edema Its presence may be inferred when there is heart disease The usual manifestations are (1) a decrease in the vital capacity, (2) the presence of heart failure cells in the sputum and (3) the characteristic roentgen ray picture Bronchitis frequently occurs causing cough and mucopurulent sputum Occassionally the symptoms of congestion are misinterpreted The clinical history of mitral stenosis

is often strikingly like that of pulmonary tuberculosis severe cough profuse sputum shortness of breath recurring hemoptysis and often loss of weight and a little fever I have seen good physicians overlook the mitral stenosis and such cases are occasionally sent to tuberculosis sanatoriums In emphysema and chronic bronchitis myocardial insufficiency gradually develops and when patients are observed for the first time in the stage of severe myocardial insufficiency the pulmonary symptoms often are ascribed to congestion alone and the cardiac condition is regarded as the primary disease The true sequence of events may be unsuspected until autopsy reveals the absence of valvular and myocardial disease and the presence of tremendous hypertrophy and dilatation of the right heart

The *treatment* of passive congestion is the treatment of the underlying cardiac condition together with the usual remedies employed to mitigate the symptoms of the associated bronchitis

Hypostatic Congestion

In patients with weakened heart action who remain for a long time in one position congestion occurs in the dependent parts of the lungs and serum exudes into the alveoli The same conditions favor the development of areas of atelectasis and the combination of edema and atelectasis gives the typical picture of hypostatic congestion The lungs become firm and tough and the alveoli are filled with a sero sanguinolent exudate that gives the affected parts a deep brownish red color the consistency and the color giving rise to the term splenization Hypostatic congestion occurs in exhausting febrile conditions especially typhoid fever in heart disease in cachectic states in late stages of chronic diseases and with special frequency in old people who for any cause are long confined to bed

Cyanosis and dyspnea of varying grade are the usual symptoms Cough and sputum often blood streaked are frequently present The percussion note at the bases is dull The breath sounds are diminished in intensity or distant and blowing in quality the voice sounds intensified and bronchial in quality Numerous moist *rales* usually accompany inspiration If the condition causing the hypostatic congestion is recovered from the edema and congestion rapidly subside and the collapsed lung is again distended If on the other hand the hypostatic congestion persists for a long time infection occurs and bronchopneumonic areas

The distended capillaries may actually be seen protruding into the alveoli and diminishing their lumen The dilated vessels also reduce the resiliency of the lungs and if the congestion lasts a long time fibrous tissue grows in the alveolar walls and further impairs the elasticity Which of these two factors is the more important it is impossible to say, but probably in the early stages of congestion the space-filling effect of the engorged blood predominates and at later stages the rigidity of the lungs plays an increasingly important role

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of the lung preceded the enlargement and terminal dilatation of the right side of the heart Certainly with massive pulmonary edema there is obstruction to the flow of blood with a rise in pulmonary arterial pressure owing to the fact that the right side of the heart is working against an abnormally large bed of fluid In such cases dilatation of the right side of the heart naturally follows rather than precedes the development of pulmonary edema as had been assumed by some earlier workers

The edema fluid itself is a plasma filtrate high in protein content In severe cases blood is present The absence of clotting has been shown to be due to the lack of fibrin

Physiological disturbances that accompany the pathological changes mentioned above are of great importance With the onset of pulmonary edema there is decreased aeration of the alveoli and oxygenation of the blood Anoxia in turn promotes increased capillary permeability with added pulmonary edema This sequence of events produces a vicious circle Since the edema extends to the lymphatics as already noted pulmonary exudates and transudate are inadequately cleared With pulmonary edema and consequent anoxia there may be increased venous return and increased cardiac output but in general the peripheral circulation has been found to be normal

It should be said however that there are many discrepancies between clinical observations and the usual explanations of the etiology Adequate experimental data to explain the syndrome fully are still lacking and the older theories of left ventricular failure and pulmonary back pressure are also at present totally inadequate to explain the true sequence of events

Etiology It is probable that a wide variety of causes exists in the production of pulmonary edema Among these may be listed

Mechanical Cardiovascular diseases are the commonest in this category Among them are hypertension and cardiac failure aortitis and aortic regurgitation coronary thrombosis mitral stenosis pericarditis wounds of the heart and cardiac aneurysm Pulmonary embolism is also a mechanical cause as are certain chronic pulmonary diseases such as tumor tuberculosis and other chronic infections

Inflammation as in pneumonia causes pulmonary edema Other infections listed have been scarlet fever and whooping cough Fever itself through acute circulatory changes has been cited as a cause by Freedberg and Altschule[6]

of inflammation develop a condition spoken of as hypostatic pneumonia This is a frequent cause of death in long standing cardiac disease and in all chronic diseases The advent of infection is often difficult to appreciate Fever is the safest guide although it is seldom high and is sometimes absent Patches of consolidation may be outlined over the lower lobes Cyanosis dyspnea and cough may become aggravated Hypostatic bronchpneumonia usually is fatal quickly

Treatment In hypostatic congestion the circulatory conditions must be carefully watched and when there is need supported by appropriate remedies In all protracted illness especially when the patient is comatose or somnolent regular and frequent change of posture should be ordered This is particularly important in old people after operation and they should be gotten into a sitting posture and out of bed as soon as conditions will permit When pneumonia develops sedatives and expectorants may be used in addition to heart stimulants

Edema of the Lungs

When serous fluid exudes from the pulmonary capillaries into the surrounding connective tissue the alveoli and the bronchi the condition is called pulmonary edema The exudation may occur suddenly or it may come on gradually in association with chronic passive congestion Clinically it is difficult to distinguish sharply between passive congestion and edema because the one merges gradually into the other and the two are nearly always combined We cannot detect edema until fluid seeps into the alveoli, but before the fluid reaches the alveoli it must permeate the connective tissue framework around the blood vessels The stage at which the connective tissue holds the fluid but none has yet reached the alveoli is spoken of as *latent edema*, the stage at which fluid has entered the alveoli is *manifest edema* The distinction is important for purposes of description but has no practical significance

Pathology Farber[5] has described the pathology of pulmonary edema in rabbits following cervical vagotomy Massive pulmonary edema occurred with bloody fluid and slight dilatation of the right auricle and ventricle Edema was present in both interstitial and air spaces the latter showing albuminoid linings and casts The pulmonary vessels were tremendously dilated the veins capillaries and lymphatics more dilated than the arterioles Red petechiae of consolidation on the surface

of the lung preceded the enlargement and terminal dilatation of the right side of the heart Certainly with massive pulmonary edema there is obstruction to the flow of blood with a rise in pulmonary arterial pressure owing to the fact that the right side of the heart is working against an abnormally large bed of fluid In such cases dilatation of the right side of the heart naturally follows rather than precedes the development of pulmonary edema as had been assumed by some earlier workers

The edema fluid itself is a plasma filtrate high in protein content In severe cases blood is present The absence of clotting has been shown to be due to the lack of fibrin

Physiological disturbances that accompany the pathological changes mentioned above are of great importance With the onset of pulmonary edema there is decreased aeration of the alveoli and oxygenation of the blood Anoxia in turn promotes increased capillary permeability with added pulmonary edema This sequence of events produces a vicious circle Since the edema extends to the lymphatics as already noted pulmonary exudates and transudates are inadequately cleared With pulmonary edema and consequent anoxia there may be increased venous return and increased cardiac output but in general the peripheral circulation has been found to be normal

It should be said however that there are many discrepancies between clinical observations and the usual explanations of the etiology Adequate experimental data to explain the syndrome fully are still lacking and the older theories of left ventricular failure and pulmonary back pressure are also at present totally inadequate to explain the true sequence of events

Etiology It is probable that a wide variety of causes exists in the production of pulmonary edema Among these may be listed

Mechanical Cardiovascular diseases are the commonest in this category Among them are hypertension and cardiac failure aortitis and aortic regurgitation coronary thrombosis mitral stenosis pericarditis wounds of the heart and cardiac aneurysm Pulmonary embolism is also a mechanical cause as are certain chronic pulmonary *diseases* such as tumor tuberculosis and other chronic infections

Inflammation as in pneumonia causes pulmonary edema Other infections listed have been scarlet fever and whooping cough Fever itself through acute circulatory changes has been cited as a cause by Freedberg and Altschule[*]

Chemical irritation Contact with toxic gases not infrequently causes acute pulmonary edema Carlisle[4] has listed them as follows oxides of nitrogen phosphorus trichloride phosphorus pentachloride, methyl bromide cadmium and dust from certain alkaloids

Neurogenic causes The importance of the nervous system in the production of acute pulmonary edema cannot be overemphasized An increasing number of experimental and clinical studies are appearing that stress the importance of fundamental nervous system alterations leading to the production of this syndrome For an excellent discussion of some of the more recent work on this phase of the subject the reader is referred to the articles by Henneman

In addition many miscellaneous causes of pulmonary edema are listed most of which have their origin on a neurogenic basis Among them paracentesis may be mentioned This procedure has been known to produce acute pulmonary edema especially when large amounts of fluid are suddenly withdrawn from the pleural or abdominal cavities Uremia and toxemias of pregnancy have on occasion been followed or accompanied by pulmonary edema Alcoholism and venoms are also listed as causes

Agonal Pulmonary Edema It is commonly recognized that shortly before death from any chronic disease especially from nephritis hyper tension myocardial insufficiency tumors and acute infections the signs of vaso-congestion become evident followed by generalized pulmonary edema As a rule this heralds the rapid approach of death and is not the cause of death but the expression of a failing circulation As Louis Hammon has said quoting Cohnheim The patient does not die of pulmonary edema—he has pulmonary edema because he is dying'

Treatment The treatment of pulmonary edema is essentially the treatment of the condition to which it is secondary Bleeding is often of value in acute pulmonary edema especially when associated with mitral valve disease or hypertension In patients with hypertension vasodilators sometimes are beneficial

Luisada[9] properly points out that drug therapy as presently used is often irrational and may be harmful Certainly if the stimulating drugs such as digitalis coramine and caffeine are used the sedative drugs are often antagonistic Followers of the heart failure theory may be justified in the use of digitalis in recurrent attacks when it is clearly recognized that a failing heart may be the cause of the condition, but digitalis in acute pulmonary edema of other cause cannot be expected

to be of benefit Of the sedative drugs the barbiturates in relatively small doses may be useful in allaying apprehension but probably have no further effect Morphine is contraindicated as in all pulmonary conditions in which cough is essential to rid the lungs of excessive secretions

Unquestionably oxygen is the most important treatment for pulmonary edema When this condition develops respiratory and circulatory decompensation have occurred and anoxia has already become evident As previously explained the vicious circle has been set up and must be broken It is of course more easily broken early in the course of the disease and oxygen therapy at that time probably has its most important place in the prevention of pulmonary edema Hinshaw[4] believes that oxygen should be used in the treatment of pneumonia wherever respiratory decompensation begins to be evident and frequently before any such evidence appears If the development of cyanosis dyspnea and increasing moist *rales* is awaited before oxygen treatment is begun it may be too late to prevent the development of irreversible pulmonary edema

Whether oxygen should be administered by means of a tent an intra nasal catheter or a mask must be determined by local circumstances and the choice of the physician Since it is difficult however to preserve a concentration of oxygen in an excess of 60 per cent by means of the ordinary tent or by means of an intra nasal catheter it is probable that an efficient oxygen mask should be preferred in most cases to the other two methods With an efficient mask concentrations approaching 100 per cent may be obtained without much difficulty and such high concentrations are frequently desirable in the treatment of pulmonary edema The accumulation of edema fluid in the smaller air passages may produce serious mechanical destruction Whenever such obstruction appears to be an important factor in preventing the uptake of oxygen it is probable that an oxygen helium combination should be considered Hinshaw[4] remarks that a number of patients have been treated in this manner at the Mayo Clinic and that improvements seem to ensue

The use of oxygen under pressure as described by Bickerman and Beck[3] has marked a notable advance in the treatment of pulmonary edema Adequate machines can now be obtained for administering oxygen under presure and the conventional anestesia apparatus may be used as employed by anesthetists Pressures not to exceed 5 to 10 cc of water may be supplied in this way for from 30 to 60 minutes but caution should be observed to be certain that the pressure does

not become too great and if an anesthesia machine is used the assistance of a trained anesthetist should be sought *It is now recognized that* respiration under positive pressure has a beneficial effect in the treatment of pulmonary edema but that since the increased intra thoracic pressure may interfere with filling of the right side of the heart less blood is able to return At the same time the left side of heart is able to propel blood out of the thoracic cavity and thus the tendency to accumulation and pooling of blood within the pulmonary circulation is lessened Respiration under an excessive degree of positive pressure at such times could therefore result in inadequate filling of the right side of the heart, with pulmonary embarrassment Moreover, it has been mentioned that since the intra thoracic pressure is decreased to pathological levels in pulmonary edema the increase in intra alveolar pressure while the patient is under positive pressure respiration, may be of marked benefit *in overcoming this condition Respiration in these circumstances prob*ably produces an intra pulmonary effect similar to that produced when an elastic stocking is worn by one suffering from varicose veins or an edematous leg The unquestionable fact that oxygen can be supplied directly and in a most concentrated form as well as in adequate volume has led to rapid clinical improvement for now large amounts of oxygen are forced into the lungs past the obstructing fluid and into the alveoli where uptake is facilitated Nevertheless it should be mentioned that positive pressure respiration is fatiguing and if possible apparatus designed to release the pressure on expiration should be used Without such an apparatus periods of unobstructed respiration are essential

Embolism Thrombosis, and Infarction

Pulmonary Embolism

In recent years the subject of pulmonary embolism has awakened renewed interest among physicians especially among those concerned *with diseases of the heart and the blood* vascular system The important advances in prevention diagnosis and treatment have led to a more hopeful attitude and an appreciation of the clinical importance of this disease Those interested in pulmonary maladies have been aroused because of problems of diagnosis and surgeons have been stirred by the possibilities offered by newer methods of therapy

The incidence of pulmonary embolism is probably higher than is commonly believed It has been stated that approximately 6 per cent of all postoperative deaths are due to this disease Barnes[1 13] who quotes McCartney as saying that the incidence of 14 000 necropsies was 2 72 per cent has estimated that approximately 34 000 persons succumb each year to pulmonary embolism There is good reason to believe that a third of these deaths could be prevented by modern methods of treatment

Diagnosis Those who have suffered non fatal attacks of pulmonary embolism are candidates for future attacks and their case histories are of great importance in diagnosis It is essential however to recognize attacks in those who have never previously suffered from this disease so that proper treatment may be instituted without undue delay

Fortunately the symptoms of pulmonary embolism are sufficiently characteristic to permit a clinical diagnosis with reasonable accuracy in the great majority of cases No symptom is pathognomonic It is a combination of symptoms following in the wake of a history which suggests that embolism has actually occurred This does not mean that roentgenographic and electrocardiographic studies are unimportant often they give extremely useful information but in most cases they are not diagnostic Physical examination likewise is seldom diagnostic

Emboli that reach the lung are nearly always bits of thrombi lodged in the right side of the heart or in the systemic veins Although other types of emboli do occur the ones of chief importance are fat emboli and air emboli which will be considered separately

Predisposing factors Pulmonary embolism is promoted by venous injury and venous stagnation as well as by abnormal coagulability of the blood These factors usually acting in combination with each other appear to cause intravascular clotting which is the precursor to pulmonary embolism

It is well known that intra abdominal or pelvic operations in which there is much trauma to the tissues and in which large veins are injured may be followed by pulmonary embolism This is especially true if there is infection subsequent to the operation The disease more frequently follows operations involving the lower abdomen than it does those that involve the upper abdomen — unlike atelectasis in which the reverse is true Both embolism and atelectasis are rare after operations upon the head neck and extremities Embolism appears more often following splenectomy than after any other operation although whether this is due to the operation itself or to the associated disease

not become too great and if an anesthesia machine is used the assistance of a trained anesthetist should be sought It is now recognized that respiration under positive pressure has a beneficial effect in the treatment of pulmonary edema but that since the increased intra thoracic pressure may interfere with filling of the right side of the heart less blood is able to return At the same time the left side of heart is able to propel blood out of the thoracic cavity and thus the tendency to accumulation and pooling of blood within the pulmonary circulation is lessened Respiration under an excessive degree of positive pressure at such times could therefore result in inadequate filling of the right side of the heart, with pulmonary embarrassment Moreover it has been mentioned that since the intra thoracic pressure is decreased to pathological levels in pulmonary edema the increase in intra alveolar pressure while the patient is under positive pressure respiration, may be of marked benefit in overcoming this condition Respiration in these circumstances probably produces an intra pulmonary effect similar to that produced when an elastic stocking is worn by one suffering from varicose veins or an edematous leg The unquestionable fact that oxygen can be supplied directly and in a most concentrated form as well as in adequate volume has led to rapid clinical improvement for now large amounts of oxygen are forced into the lungs past the obstructing fluid and into the alveoli where uptake is facilitated Nevertheless it should be mentioned that positive pressure respiration is fatiguing and if possible apparatus designed to release the pressure on expiration should be used Without such an apparatus periods of unobstructed respiration are essential

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the right ventricle at the site of a myocardial infarct due to the occlusion of a branch of the coronary artery

Thrombosis in the systemic veins is frequently followed by pulmonary embolism Almost invariably from this source come the large emboli that cause grave symptoms and sudden death Frequently the venous thrombosis is unsuspected until pulmonary embolism occurs Often the signs of femoral thrombosis appear only after pulmonary embolism has taken place The causes of venous thrombosis cannot be discussed here They are varied and many of them obscure It occurs frequently with all infectious diseases although much more commonly with some than with others It often follows operation even when infection is absent After childbirth there is extensive thrombosis of the uterine venous sinuses and the pelvic veins often become thrombosed even when there is no evidence of infection Sometimes phlebitis and venous thrombosis occur independently of any other apparent disease Stasis in the venous circulation is often associated with thrombosis sometimes with sometimes without added infection Certain diseases of the blood — for instance chlorosis — predispose to clotting and are often accompanied by venous thrombosis In all of these conditions pulmonary embolism may occur but clinically it is observed particularly in connection with disease of the heart after infectious diseases and after operation and childbirth

Pulmonary embolism may occur almost simultaneously with the formation of the venous thrombus the whole thrombus or parts of the thrombus becoming detached and being carried to the lungs If we assume that venous thrombosis occurs at the time of operation then from the seventh to the fourteenth day after the formation of the thrombus is the usual time for embolism to occur This same time relation apparently exists in venous thrombus due to infectious diseases Following trauma it seems to come later than after operation Embolism may occur during the third week following operation or after childbirth and these late emboli are often larger Emboli go much more frequently to the lower than to the upper lobes and more often to the right than to the left lower lobe

When a branch of the pulmonary artery is occluded an infarct is often produced The pulmonary arteries are terminal arteries but there is a free anastomosis between the capillaries of the different branches and the bronchial artery nourishes the bronchi and the adjacent pulmonary tissue This free anastomosis is sufficient to prevent the occurrence of infarction in normal lungs even when large branches of the pulmonary

of the hemopoietic system is not known Explorations in cases in which inoperable carcinoma is found are also dangerous from the standpoint of embolism In general the incidence of postoperative embolism parallels the magnitude of the surgical procedure the complications being twice as frequent in bilateral hernioplasty as in unilateral, and so on

Aside from operations the stagnation of venous blood may result from increasing age from prolonged physical inactivity as in debilitating diseases obesity and diseases of the circulartory system The fact that age is an important factor is shown by the rarity of the disease before 40 and its increasing frequency thereafter As we said earlier, the disease is common in those who have suffered prior attacks but may appear *de novo* in obese people or in those in the older age groups who have been confined to bed for long periods particularily if they are suffering from metastatic malignancy, cardiac disease or varicose veins

Thrombophlebitis predisposes to pulmonary embolism Fortunately however, in peripheral thromophlebitis the thrombus is usually so fixed by inflammation that the massive pulmonary embolism in such cases is rare More commonly the emboli are small and non fatal Indeed the phenomena of pulmonary embolism if such occur are more frequent a few days before the symptoms of thrombophlebitis appear than after the condition is well established This observation is probably important clinically since it confirms the belief that prolonged periods of inactivity after the appearance of thrombophlebitis are unnecessary if they are prescribed in the hope of avoiding future embolism Quite the reverse would seem to be the case Priestly and Barker[30] reported an incidence of pulmonary embolism in per cent of 938 cases of thrombophlebitis but in only 4 4 per cent of cases did the embolism appear later than six days after the diagnosis of thrombophlebitis

Postoperative emboli may occur at any time during the first four weeks following surgery About one fourth of the cases will occur during the week subsequent to operation about one half in the second week and the remaining quarter in the third and fourth weeks

Pulmonary embolism is particularly common in heart disease associated with distention of the right side of the heart At autopsy mural thrombi are found in the auricular appendage or lodged among the papillary muscles They occur with especial frequency in mitral stenosis but are not uncommon in other forms of myocardial insufficiency Pulmonary embolism often follows the development of a thrombus in

following pulmonary embolism but without destruction of tissue (3) The infarct in which the circulation is so seriously impaired that not only does hemorrhage occur but also the pulmonary tissue becomes necrotic The first type may rapidly come and go with the degree of pulmonary congestion the second may be absorbed leaving the lung tissue normal the third in which the tissue is destroyed is replaced by a scar If the infarct becomes infected abscess and gangrene may occur The proximity to the pleural surface may lead to empyema and pneumothorax

The *symptoms of pulmonary embolism* depend upon the size of the artery that is occluded If the embolism occludes the trunk of the pulmonary artery or both main branches death occurs almost instantly Occlusion of both the right and left pulmonary artery is usually produced by a large embolus straddling the bifurcation and projecting into both vessels A patient convalescing from an infectious disease or from childbirth sits up in bed or gets up for the first time and suddenly falls over pale and unconscious and after a few gasps is dead Or the patient is suddenly seized with extreme dyspnea struggles for breath becomes pale or cyanotic may call for help or say a few words and becomes unconscious while pulse and respiration rapidly fail When a large embolus passes the bifurcation it lodges usually in the right main branch of the pulmonary artery If the patient s condition is good and the circulation unimpaired he does not die suddenly Death may come hours later with cardiac failure but recovery often follows The patient suddenly becomes extremely dyspneic and presents the clinical picture of profound shock The pulse is rapid and small the skin pale or cyanotic and cold is bathed in sweat the features portray mortal anxiety The patient may continue to struggle for breath as the pulse grows weaker and weaker and finally with a rapidly failing circulation become unconscious and die but often the symptoms gradually abate and slowly disappear The patient may then seem to be well but the pressure in the pulmonary circulation may remain high and months or years later myocardial insufficiency may develop with great hyperthrophy and dilatation of the right ventricle

It is not difficult to understand how sudden death occurs when the trunk of the pulmonary artery or both main branches are occluded The pulmonary circulation is then completely cut off no blood reaches the left side of the heart and cerebral anemia at once ensues But the mechanism that produces the grave symptoms always accompanying the occlusion of one main branch the sudden death that occasionally occurs

artery are occluded Virchow[3] in his classical experiments, succeeded in producing pulmonary infarcts only when he introduced infected material into the pulmonary artery For the occurrence of pulmonary infarction there must be in addition to embolism some circulatory disturbance in the lung or some injury to the lung tissue This combination of circumstances is found particularly in the presence of passive congestion

Pulmonary infarcts produce in the lungs firm dark red masses of a triangular pyramidal form They are dry and often remarkably hard and since the base usually reaches the pleural surface they are elevated and easily discernible The pleural surface over the infarct is roughened Sterile pleural effusion frequently occurs At the apex of the infarct the embolus can usually be seen lying in the pulmonary artery Microscopically the alveoli and all of the tissues in the involved area are packed with blood

Some infarcts are replaced by dense scar tissue when they heal, others are absorbed and the function of the affected portion of the lungs is restored That this restitution occurs cannot be doubted for it is observed frequently in the clinic I have again and again seen a whole lobe infarcted and yet a few months later neither physical examination nor the roentgenogram disclosed any abnormality whatsoever This is somewhat remarkable since infarcts occur only when the blood supply to tissue is cut off and when the blood supply is diverted the tissue dies But in the lungs the arrangement of the circulation is different from what it is elsewhere in the body I have already pointed out that under normal conditions no infarct forms in the lung when the main pulmonary artery or one of its branches is occluded An infarct develops only when in addition the circulation is otherwise impaired and it is impaired in most of the circumstances when embolism occurs namely in heart disease during infectious diseases and following operations From what we observe clinically we conclude that it requires but little change in the circulation to determine whether an infarct will form or will not form The extravasation of blood comes from the pulmonary artery but although the alveoli may be gorged with blood the fact that the tissue does not die suggests that it is satisfactorily nourished through the bronchial artery and its branches We must therefore recognize three types of infarction (1) The congestion infarct which is a localized accumulation of blood that exudes into the alveoli in congestion without occlusion of the pulmonary artery Properly speaking this is not a true infarct (2) The infarct due to the extravasation of blood

following pulmonary embolism but without destruction of tissue (3) The infarct in which the circulation is so seriously impaired that not only does hemorrhage occur but also the pulmonary tissue becomes necrotic The first type may rapidly come and go with the degree of pulmonary congestion the second may be absorbed leaving the lung tissue normal the third in which the tissue is destroyed is replaced by a scar If the infarct becomes infected abscess and gangrene may occur The proximity to the pleural surface may lead to empyema and pneumothorax

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and the delayed death that is not uncommon is not fully understood In animals death from pulmonary embolism occurs only when the main pulmonary artery is occluded Plugging one of the two main branches causes an elevation of the pressure in the pulmonary artery and a transient fall of aortic pressure It has usually been assumed that some reflex action leading to cardiac standstill or respiratory paralysis plays an important part in causing the symptoms of pulmonary embolism to appear followed by sudden death Careful animal experiments however have failed to reveal any evidence of such a reflex action It is altogether likely that the outcome of occlusion of one of the main branches of the pulmonary artery depends entirely upon circulatory efficiency If the condition of the circulation is normal and the heart healthy recovery will invariably take place If the circulation is impaired or the heart enfeebled by disease death may come suddenly or after hours or days depending upon whether the heart fails at once or more slowly to meet the added demand put upon it Clinicians have commented upon the fact that death from pulmonary embolism occurs more commonly in patients past middle life than it does in the young

When the embolus passes the main branch of the pulmonary artery and lodges in one of the large subdivisions a different train of clinical symptoms is evoked With the lodging of the embolus there is suddenly severe pain followed at once by a rapid rise in the pulse rate by cyanosis and by dyspnea These symptoms gradually subside but are usually followed in from 24 to 48 hours by the symptoms of pulmonary infarction In patients in a weakened condition especially in those with myocardial disease such emboli may be followed by rapidly fatal cardiac failure With the development of a pulmonary infarct there is usually pain in the side cough and bloody sputum The temperature rises and there is dullness diminished or blowing breath sounds fine moist *rales*, or a pleural friction usually over the right lower lobe This group of symptoms often leads to the diagnosis of pneumonia The fever usually lasts from eight to ten days falling gradually to normal At times the temperature-pulse relation is so characteristic that a glance at the bedside chart is sufficient to make the diagnosis After operation let us say the temperature and pulse rate are normal or as is usually the case a little elevated Suddenly the patient has a sharp pain in the chest and the pulse curve rises abruptly from 80 to 120 The temperature curve remains at the normal level but at the end of from 24 to 48 hours the temperature gradually rises as the pulse curve slowly falls Temperature and pulse then both remain high for six or eight days and then

both gradually fall again to normal The sputum of infarction is quite characteristic although the same type of sputum occurs in other conditions It is a bloody sputum dark and evenly colored Frequently more or less *fluid blood* is mingled with the masses of bloody sputum

When the embolus plugs a small branch of the pulmonary artery only slight symptoms are produced If no infarct forms the accident may pass unnoticed If a small infarct forms there is pain in the side lasting for a few hours or a few days bloody sputum and usually a little fever Bloody sputum occurs in from 8 to 24 hours after the infarction If numerous small infarcts occur at the same time or nearly simultaneously symptoms are produced similar to those caused by occlusion of a large vessel Such an occurrence however is exceedingly rare Small infarcts usually give no physical signs at most they are accompanied by showers of fine crisp pleural *rales* over the area of pain Larger infarcts may give a little dullness and slight changes in the character of the breath sounds

When infected emboli reach the lung they produce in addition to the mechanical changes the usual results of infection The emboli are often multiple and give the characteristic clinical picture of septic pneumonia encountered so typically in postpartum streptococcus infection If the infarct is single an abscess may form Empyema and gangrene are less common Pulmonary emboli occur commonly in Streptococcus viridans endocarditis the emboli coming from vegetations in the right heart or from mural thrombi (as in nonbacterial valvular heart disease) or from thrombi in the peripheral veins Even when the Streptococcus viridans is present in the emboli suppuration does not occur and the infarcts progress as do bland infarctions Pleural effusion usually of slight or moderate extent commonly follows pulmonary infarction despite the fact that the emboli may be uninfected

The *diagnosis* of pulmonary embolism is not difficult if the possibility of it is held in mind I am convinced that it occurs far more frequently than is usually stated In my experience many postoperative pleurisies and postoperative pneumonias (so called) are really the effects of pulmonary embolism During convalescence from infectious diseases sudden death or the abrupt onset of circulatory symptoms of collapse are far more commonly due to pulmonary embolism than to primary cardiac failure although they are usually ascribed to the latter cause There are a few important points in this connection which should be emphasized (1) Venous thrombosis is extremely common after all operations especially after abdominal and pelvic operations even though the operation

is 'clean' and convalescence uneventful These thrombi usually pass unrecognized unless pulmonary embolism occurs (2) Venous thrombosis occurs commonly in infectious diseases particularly in pneumonia and typhoid fever It often passes unrecognized clinically (3) Venous thrombosis is the commonest cause of a little 'unexplained' fever persisting through convalescence from operation or an infectious disease (4) Extensive pulmonary embolism and infarction may occur without the patient s having bloody sputum or indeed any sputum (5) In patients convalescing from operation or infection sudden pain in the chest associated with simultaneous acceleration of the pulse rate and accompanied a little later by fever and the physical signs of pleurisy consolidation or pleural effusion almost always means pulmonary embolism Characteristic bloody sputum when it occurs certifies the diagnosis (6) Small pulmonary emboli frequently precede larger fatal emboli An appreciation of these warning symptoms may sometimes avoid grave accidents

Abdominal pain is mentioned as a prominent feature of pulmonary embolism in some instances but in my experience this has been rare When it occurs it is overshadowed by the thoracic pain and is in fact in most instances an extension of the thoracic pain over the upper abdomen Nevertheless the upper abdominal manifestations may include tenderness and even board like rigidity and lead to the suspicion that some upper abdominal catastrophe has taken place although the total clinical picture usually develops so rapidly that one is not long left in doubt The upper abdominal symptoms usually recede rapidly, leaving more or less localized chest pain in their wake

At times the symptoms may suggest acute cardiac disease and lead to the erroneous assumption that the entire condition is primarily cardiac Massive pulmonary embolism leads to the dramatic appearance of acute cor pulmonale in which the right ventricle is suddenly called upon to force the full stream of blood through a channel narrowed by the presence of the embolus In my experience however the dramatic onset itself usually precludes error in such cases

The condition may be more difficult to recognize when cardiac strain is less evident Such cases may manifest themselves by dyspnea and palpitation gallop rhythm and increased pulse rate but accompanying symptoms normally suffice to clear up the diagnosis In fact, as in other fields of internal medicine the important thing is for the clinician to have the possibility of pulmonary embolism in mind and to be ready to confirm the diagnosis by electrocardiographic and roentgen

evidence of patients who develop nervousness apprehension and palpitation followed by pleural pain blood spitting and sometimes pleural effusion

The electrocardiographic tracings may be highly characteristic of acute right ventricular strain While these may be confused at times with the findings of posterior left ventricular infarction there are certain differences which are usually characteristic After pulmonary embolism there is a constant S wave in lead I and the ST segment arises slightly below the base line In lead II the RST segment usually arises below the iso electric level Rarely T II is inverted In lead III a Q wave is present Also in lead III the RT segment is slightly elevated and the T wave inverted Usually there is a prominent Q wave in lead III but the other features of the Q III are absent Precordial leads are helpful the electrodes being placed near the left border of the sternum in C II and C III positions The Wolferth lead is also helpful in showing a reversal of the normally inverted T wave

Roentgenographic findings The roentgenographic findings described under chronic passive congestion are frequently present in pulmonary embolism but are more likely to be unilateral consisting of accentuation of the hilar shadow and general vascular markings when the affected side is compared to the other Elevation of the diaphragm and obliteration of the costophrenic angle are usually present on the affected side Mottled or patchy infiltration may be present also or one or more areas of infiltration suggesting bronchopneumonia

Treatment Massive pulmonary embolism is a medical emergency demanding the most immediate and vigorous treatment available Oxygen in high concentrations is always indicated and for this purpose should be given by mask since the usual tent permits concentrations of only 50 or 60 per cent It is doubtful if cooling is of any advantage in such situations since cold air may be a factor in promoting vasoconstriction

Drug therapy is of definite value in all but the most massive cases of pulmonary embolism Pain and respiratory distress can be controlled by the use of morphine and circulatory failure by the use of appropriate stimulants and digitalis As early as 1927 Barnes[1 13] advocated the use of papaverine and this drug has gained wide acceptance especially when the condition is accompanied by arterial occlusion of the extremities Certainly there is experimental evidence that the drug combats reflex constriction of vessels in the pulmonary circulation Barker[30] recommends the intravenous administration of 0 32 gm of papaverine and

00065 gm of atropine as soon as possible after the diagnosis of massive pulmonary embolism has been made If morphine has been administered however the synergistic effects of the two drugs should be kept in mind Since papaverine and atropine should be administered intravenously in view of the urgency of the situation it is probable that they should be readily available *in all surgical wards They are the most effective agents* in combatting vasospasm and bronchospasm mediated by way of the vagus nerves Regardless of other drugs employed atropine should be used consistently in full dosage

Heparine and dicumarol The treatment of pulmonary embolism should also be directed toward the prevention of further thrombosis at the site from which the original embolus was released and toward the prevention of a propagating thrombus within the pulmonary vessels To accomplish this end 50 mg of heparin may be given immediately to affect rapidly the coagulability of the blood At the same time 300 mg of dicumarol may be given since the effect of this drug on the prothrombin time is not immediate For the first 24 to 36 hours heparin should be relied upon

Heparin has the advantage of being rapid in action and if hemorrhage is feared it has the additional advantage of relatively brief action This latter characteristic however demands frequent intravenous administration or a continuous drip Since it is desirable to maintain the coagulation time of the blood at a value of from fifteen to twenty minutes the frequency of intravenous injections should be not over three *or four hours if this method is chosen Depoheparin may be preferred,* the effect of this drug lasts about 12 hours but does not otherwise differ from heparin

Dicumarol *the product of spoiled sweet clover may be taken by* mouth in an initial dose of 300 mg as stated followed by doses of 200 mg daily if the prothrombin time is less than 35 seconds If the prothrombin time is found to be in excess of 35 seconds on any given day the dose should be omitted for that day Since the required dosage may vary in individual patients a smaller amount than that stated may be found to be sufficient

It should be remembered that dicumarol therapy carries with it the danger of hemorrhage unless the dose is accurately determined This is done by frequent determinations of the prothrombin time by the Magath *modification of the Quick method* With proper attention to this precaution the treatment is relatively safe since thrombosis rarely occurs

if the prothrombin time is greater than 27 seconds (normal is 17 to 19 seconds) and hemorrhage is rare if the prothrombin time is less than 60 seconds It is recommended that the prothrombin time be maintained within these limits

Dicumarol has the advantages that it can be taken by mouth and that its action is prolonged but it has the disadvantage that hemorrhage may occur unless the safeguards mentioned above are rigidly observed In the event of hemorrhage however the transfusion of normal blood will overcome this tendency quite promptly although temporarily In the event of excessive elevation of prothrombin time it may be shortened by large doses of synthetic Vitamin K

The use of anticoagulants in the prevention of postoperative pulmonary embolism deserves consideration but should probably be reserved for those facing unusual hazards such as patients who have a previous history of pulmonary embolism or thrombophlebitis those who *are exceptionally obese or those in the older age groups who face operations* known to be hazardous from this standpoint

Fat embolism occurs chiefly after extensive injury to the bones it occurs rarely in disease or injury of fatty tissue elsewhere in diabetes or in phosphorous poisoning The condition seldom can be diagnosed clinically but may be suspected if cyanosis and dyspnea follow shortly after injury to the bones It may play a part in the production of the symptoms of shock following such an injury

The frequency with which fat embolism follows fractures is variously estimated by different observers Some contend that it occurs even after simple fractures in at least one half of the cases No clinical symptoms appear by which it may be recognized the diagnosis being made by finding fat in the sputum and urine Many doubt that this evidence justifies the diagnosis Fatal fat embolism is occasionally observed following the introduction of oil into the circulation Hamman reports an instance at the Johns Hopkins Hospital in which sounds were passed in an effort to dilate a urethral stricture The attempt was unsuccessful and no doubt the mucous membrane of the urethra was injured by the trauma About 30 or 40 cc of mineral oil were then forcibly injected into the urethra and the pressure was maintained by holding the urethra closed near the meatus A few days later the patient died and at autopsy universal fat embolism was found The same condition has occasionally followed the intravenous injection of arsphenamine when no oil has been introduced with the *solution It is not understood how the injec*

tion of arsphenamine brings about fat embolism In these conditions fat emboli are distributed throughout the body, and the occlusion of the pulmonary arterioles is but a part of the general plugging of these vessels The patients usually present the symptoms of shock and although bizarre and unusual manifestations may occur additionally, neurological symptoms generally predominate

Dunphy and Ilfeld[18] list three conditions necessary for the development of fat embolism (1) liquid fat free in tissues (2) torn and patent veins and (3) increased local tissue pressure above the level of venous pressure These conditions may arise after fractures, blast injuries burns extensive contusions of subcutaneous tissues or surgery

The condition should be suspected when injuries to bone even simple fractures of the tibia or femur or extensive soft tissue injuries or surgical procedures in which large amounts of fat are traumatized, are followed by an interval free of symptoms from a few hours to ten days and then by the onset of pulmonary or cerebral symptoms Pulmonary manifestations may vary from moderate elevation of the respiratory rate with little fever to severe pulmonary edema Cerebral manifestations may be mild with slight confusion or severe with clonic convulsions rigidity and coma When both sets of symptoms appear after a free interval the diagnosis is unmistakable Petechiae may appear in the skin In severe cases fat may be found in the urine and sputum Chest films are not diagnostic their findings resembling those seen in acute pulmonary edema

Although treatment is thought to be useless oxygen in high concentrations as described under treatment of other types of embolism is probably indicated

Air Embolism Small amounts of air may enter the circulation without producing ill effects It is estimated that up to 100 to 150 cc of air may be necessary to produce death[19] In pulmonary air embolism air enters the circulation through a systemic vein and causes obstruction of right ventricular outflow Air entering the pulmonary veins produces arterial air embolism with obstruction of systemic arteries especially of the central nervous system and the coronary vessels

It was formerly believed that sudden death following the induction of artificial pneumothorax could be ascribed to pleural shock It is now known that such deaths are always due to air embolism and that it is not necessary to inject air since in some instances no air has been admitted and the occurrence has taken place in simple thoracentesis Deaths

have also been reported following the operation of pneumoperitoneum especially where this procedure has been employed during the later stages of pregnancy when presumably large uterine veins have been traumatized

It is known that air already present in the thoracic cavity can be an important source of air embolism if the trauma produced by the needle provides an access of air to the venous system and the pressure relationships of the source and veins are such as to allow the air to enter the circulation Air is usually present in the alveoli and in pulmonary cavities it may be present in the pleural space and may find its way into the circulation under the conditions given above

On the other hand air may be injected when a pneumothorax apparatus is employed or aspirated into the pulmonary veins during open chest procedures It is doubtful if the small amount of air present in the tubing is ever of importance Air may be injected directly into a pulmonary vein but more commonly an adhesion between the lung and the chest wall is torn with the production of a pleural venous fistula This accounts for the fact that air continues to enter the circulation even after the needle has been withdrawn It is rare for such an occurrence to take place when the pulmonary tissue is normal a fact which suggests that diseased areas should be avoided when puncturing the chest wall for the induction of pneumothorax or other purposes The clinical symptoms are usually heralded by a brief period of anxiety on the part of the patient with faintness or dizziness In severe cases loss of consciousness rapidly ensues and in about half the cases convulsions occur *During this stage the skin over the posterior portion of the body may become marbled At this stage too air may be detected in the retinal vessels or over the tongue the so called Liebermeister's phenomenon* However the demand for prompt treatment and obviousness of the diagnosis usually preclude such investigation

It is important that the head be lowered and the legs elevated at once to permit the air to accumulate in the most dependent portion of the circulation Death rarely occurs where such maneuvers are undertaken promptly By this means cerebral embolism can be avoided Coronary artery involvment can probably be lessened by placing the patient mid way between left lateral and prone since the right coronary artery arises anteriorly from the right aortic sinus and the left coronary artery arises mesially from the left posterior aortic sinus

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infection from tuberculosis histoplasmosis and similar disease, and many erode the bronchi producing hemorrhage of varying degrees With expectoration of the stone the bleeding promptly ceases In other cases the stone apparently becomes firmly fixed in its bed again and the episode passes A certain number of cases will remain ideopathic Such patients should be followed closely by x ray and in no event should be discharged without a prolonged period of observation

The *diagnosis of hemoptysis* is sometimes difficult It must be distinguished from bleeding from the upper respiratory passages and from hematemesis If there is doubt the history is usually conclusive In hemorrhage from the lung after the first hemoptysis is over the patient continues during the following 24 to 48 hours to cough up dark clots of blood Bleeding from the posterior nares may simulate hemoptysis but inspection at the time of bleeding or a careful inquiry about the symptoms will nearly always distinguish the two Profuse hemoptysis may be mistaken for hematemesis I have on several occasions seen a diagnosis of ulcer of the stomach made on the basis of profuse bleeding when subsequent observation showed the patient to have pulmonary tuberculosis Curiously enough I have never seen hematemesis mistaken for hemoptysis but no doubt the error does occur

In most cases hemoptysis needs no special *treatment* since the bleeding is seldom marked In tuberculosis the great danger is not from the loss of blood but from the extension of the tuberculosis Careful nursing is more important than the use of drugs When the bleeding is long continued or frequently repeated artificial pneumothorax will control it more promptly and more certainly than any other measure Before inducing pneumothorax the physician must determine definitely from which side the hemorrhage is coming This is often impossible Unfortunately pleural adhesions may prevent pulmonary collapse Pneumoperitoneum has also been advocated as a control for hemorrhage in tuberculosis and in some cases appears to be of great value When there is hemorrhage morphia should be avoided at all costs since it checks the cough reflexes and leads to atelectasis and in infectious cases to dissemination of the underlying disease through failure to cough up secretions It is probable that no treatment at all is preferable to too much sedation Nervousness can usually be allayed by an explanation of the situation to the patient and if necessary by the use of phenobarbital in moderate doses It is impossible to discuss in detail all of the methods that have been used to control pulmonary bleeding Some of the methods are harmful most of them without value The nitrites pitui

Hemoptysis

Hemoptysis signifies bleeding from the lungs or bronchi Even blood-streaked sputum may be included under this term although it has come to be used generally in a more restricted sense to signify the expectoration of blood Used in this sense it is equivalent to frank hemoptysis and does not embrace blood streaked or bloody sputum It is important to define what the term includes because while all conditions that cause blood spitting commonly cause also the expectoration of bloody sputum there are many conditions that are almost regularly associated with bloody sputum and yet rarely cause hemoptysis Pneumonia both lobar and lobular and chronic passive congestion of the lungs are among the most common causes of bloody sputum but seldom cause blood spitting The exceptions are chiefly certain cases of bronchopneumonia complicating virulent specific infections particularly influenza Lobar pneumonia is very rarely ushered in with hemoptysis The common causes of blood spitting are pulmonary tuberculosis and pulmonary infarction Less common causes are bronchiectasis, growths abscess and gangrene of the lung and mitral stenosis uncommon causes are trauma aortic aneurysm syphilis constitutional diseases such as purpura hemorrhagica hemophilia scurvy animal parasites particularly echinococcus and pulmonary distoma leprosy aspergillosis actinomycosis streptothricosis et cetera The presence of blood in the sputum is always an important symptom from the diagnostic standpoint It is seldom in itself of great clinical importance Large fatal pulmonary hemorrhage is uncommon and occurs only when the aorta or a large branch of the pulmonary artery is eroded or ruptures The former condition is almost always due to aneurysm the latter to pulmonary tuberculosis or malignant disease Fatal hemorrhage in tuberculosis comes usually from the rupture of an aneurysm of a branch of the pulmonary artery traversing a lung cavity

It should be borne in mind that one of the earliest signs of bronchogenic carcinoma especially in men of middle age or older is streaked sputum or hemoptysis Even in the presence of a negative chest film *these patients should be bronchoscoped promptly and if no tumor is* seen secretions obtained for examination by modern cytological techniques In women adenoma of the bronchus is frequently accompanied by hemoptysis and here again bronchoscopic search should be made even in the presence of a negative chest film

A not uncommon source of hemoptysis and a benign one as a rule is erosion of a lung stone Such stones are usually the result of past

has been described as occurring during whopping cough in children when the air travels along the vessels and may give rise to very extensive mediastinal emphysema

Pathological Anatomy

When the lungs are permanently distended they fail to collapse when the chest is opened The diaphragm has a low position and the voluminous lungs fill out the thoracic cavity and cover over the heart and mediastinum the rounded borders meeting in the midline The surface of the lungs is pale and often at the apex of base and along the margins vesicles are seen varying in size from small blebs to bullae as large as an orange Although the lungs are greatly distended they feel soft and light and indentations made by the fingers often persist The normal fine crepitation is replaced by the sensation of squeezing large bubbles Even in the substance of the lung minute vesicles may be seen formed by the rupture of distended alveoli Microscopically the alveolar walls are found to be thin and in many places broken through Torn shreds of elastic tissue may be demonstrated by special stains The capillaries are constricted and many of them are obliterated so that the area of the vascular bed is diminished The important changes therefore are three (1) great distension of the alveoli ( ) atrophy and rupture of the alveolar walls (3) obliteration of numerous capillaries

Pathogenesis

In the production of emphysema two factors must be considered (1) *increased pressure in the alveoli* (2) *the resistance of the alveolar* walls Both factors play a part but the influence of distension is usually considered the more important We might easily conceive of alveolar walls so attenuated that even the pressure of quiet breathing could gradually lead to permanent distension of the alveoli This occurs however only rarely Senile emphysema should correspond to such a hypothetical state of affairs but in senile emphysema the lungs are small and the alveoli are not enlarged It is possible nevertheless that in senile emphysema the lungs might become voluminous were they subjected to increased alveolar pressure Instances are reported of localized emphysema in the portion of a lung supplied by a branch of the pulmonary artery that has been occluded by an embolus or by arteriosclerosis These ob

tary extract, atropin calcium and the injection of serum still are frequently employed

DISEASES DUE TO ALTERATION OF ALVEOLAR LUMEN

Emphysema

The term emphysema denotes distention of the pulmonary alveoli which may be local or general When the term is used without qualifica tion, however it is usually understood to designate what is also called chronic substantive or hypertrophic emphysema This type of emphysema must be distinguished from acute compensatory, senile interstitial, and bullous emphysemas

Acute emphysema is the state of pulmonary distention that occurs with rapid deep breathing—for instance, after violent exercise, with certain forms of bronchial obstruction such as asthma and anaphylactic shock, and with other mechanical hindrances to respiration, such as laryngeal obstruction, drowning et cetera Its characteristic feature is that the lungs immediately return to their normal position when the con ditions causing the distention are removed

Compensatory emphysema is the distention of a portion of the lung due to disease obliterating another portion It occurs around atelectatic inflamed, contracted or consolidated areas in the lungs and in the oppo site lung when one is compressed or destroyed by disease

Substantive or *chronic emphysema* is a permanent irreparable disten tion of the alveoli generally though not uniformly distributed through out the lungs Acute emphysema or pulmonary distention if long maintained, leads gradually to substantive emphysema The lungs can then no longer return to the normal position even though the original cause of the distention is removed

Senile emphysema is a part of the atropic change that occurs through out the body with advancing years The alveolar walls become thinned *they often rupture and the lungs lose their elasticity In contrast to true* emphysema the lungs usually are small and retracted

Interstitial emphysema has nothing to do with other forms of emphysema The term is used to designate the conditions that arise when owing to the rupture of alveoli air enters the interstitial tissue of the lungs The air often travels to the mediastinum and from there may extend to the subcutaneous tissues of the neck and trunk This condition

has been described as occurring during whopping cough in children when the air travels along the vessels and may give rise to very extensive mediastinal emphysema

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servations suggest that at least localized emphysema may be due to primary atrophy of the alveolar walls but I think it would be extremely difficult to demonstrate that changes leading to respiratory obstruction —for instance, bronchiolar occlusion or bronchiolar spasm—had not also been present It is conceivable that changes in the pulmonary arterioles might impair the nutrition of the alveolar walls and in this way be an important factor in the development of emphysema So far as I know such an association has never been demonstrated

Although atrophy of the alveolar walls is seldom if ever the primary or sole cause of emphysema the condition of these walls must nevertheless play an important role in the ease with which the alveoli distend under increased pressure and the length of time such increased pressure may be resisted without permanent damage to the tissues composing them Experiments with elastic tissue usually strips of the aorta have demonstrated that the results of stretching depend upon the force applied and the length of time the force is allowed to act If a certain degree of stretching is maintained for a certain length of time the elastic tissue will recoil to its original length when the force is released If however a greater force acts on it for a longer time the recoil is not complete and after successive tests the tissue remains permanently stretched It seems reasonable to transfer the results of these experiments to the lungs since all of our observations indicate that both in man and in the experimental animal pulmonary tissue does respond precisely in this way It is clear therefore that the quality of the pulmonary tissue may not be ignored in considering how emphysema develops

The quality of pulmonary tissue like the quality of tissue in other parts of the body does vary no doubt in different persons Perhaps there is no way to prove this directly but it is an altogether reasonable inference Tissue superiority may be fortified by a number of correlated dispositions—in the case of the lungs for instance by the bodily conformation Some observers have tried to put these variations in precise form by claiming that elastic fibers are less numerous in emphysematous lungs than in normal lungs but the careful study of Tendeloo contradicts this contention If we estimate the difference in a rough clinical way it does seem that some patients develop emphysema more easily than others and many physicians are convinced that there is a familial tendency to the disease This is further suggested by the tendency of emphysema to appear in certain families at certain ages without other obvious antecedents I have under my care at the present time three sisters in their early forties who have all developed severe emphysema

at approximately the same age and whose mother apparently suffered from the same condition None of the patients has suffered from bronchial asthma

Even though we grant that there is a difference in the quality of pulmonary tissue this fact is relatively unimportant in the development of emphysema when compared with the effect of those changes in respiratory pressure which cause alveolar distention When this distention is maintained for a long time the lungs lose their resiliency the alveolar walls become thinned and frayed and many capillaries are destroyed These changes in turn cause grave disturbance of function the nature of which we shall soon consider For the moment we must hold our attention upon the changes in respiration which bring about long continued distention of the lungs

When a healthy person breathes rapidly and deeply as he does during violent exercise the diaphragm does not fully ascend during expiration and the lungs *do not completely* recoil but remain partly distended even at the end of expiration This may be explained by assuming that the succeeding inspiration begins before expiration is fully ended Inspiration is always an active muscular effort whereas expiration except when breathing is greatly increased is for the most part a passive recoil of the elastic chest and lungs A demand for more air therefore is promptly met by increased inspiratory effort which is not balanced by an equal increase in the force of expiration The expiratory muscles being seldom used are brought into play with difficulty and are easily fatigued This form of pulmonary distention is a normal physiological response and soon as the demand for increased ventilation ends the lungs at once return to their normal position Occasionally however the distention persists for some time after exercise is stopped and it has been suggested that this physiological distention frequently repeated may in the end lead to permanent emphysema Clinical observation of athletes and of others constantly engaged in heavy labor does not support this view Dogs breathing constantly through masks that obstruct inspiration but allow expiration to proceed unhindered do at the end of months have permanently distended lungs but the atrophic changes in the alveolar walls so characteristic of emphysema in man are not found It is possible that these too might gradually develop if the obstruction were continued for a long time

The effect of increased expiratory pressure when inspiration is unobstructed leads to pulmonary distention only when there is increased respiratory effort In coughing the expiratory pressure is suddenly

servations suggest that at least localized emphysema may be due to primary atrophy of the alveolar walls, but I think it would be extremely difficult to demonstrate that changes leading to respiratory obstruction —for instance bronchiolar occlusion or bronchiolar spasm—had not also been present It is conceivable that changes in the pulmonary arterioles might impair the nutrition of the alveolar walls and in this way be an important factor in the development of emphysema So far as I know, such an association has never been demonstrated

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lungs equally does not cause pulmonary distention unless accompanied by hyperpnea

When however we consider the results of bronchial obstruction which affects only a portion of the lungs or different parts of them unequally then the mechanism is entirely different Let us assume that one main bronchus is partly occluded the other unobstructed and that the ventilation of the unobstructed lung supplies all the respiratory needs of the individual There will then be no increase of respiration but the obstructed lung will become distended If respiration is increased by exercise the distention will become greater In quiet breathing the force of inspiration is greater than the force of expiration and while the passive recoil of the chest is sufficient to deflate the unobstructed lung it will not fully deflate the lung with the bronchus partly occluded

This fact must play an important role in the development of emphysema Experience teaches us that emphysema develops commonly as a result of chronic bronchitis and asthma In chronic bronchitis partial obstruction of bronchi due to the swelling of mucous membranes and the presence of tenacious secretion must commonly occur but this obstruction does not affect all bronchi uniformly or permanently Bronchial spasm also is unequally distributed throughout the lungs Therefore in both conditions there is unequal obstruction in different bronchi and the area of lungs supplied by the bronchi most obstructed will become distended even though there is no hyperpnea From time to time the distribution of bronchial obstruction will change and in this way different parts of the lungs will be successively distended With increased respiration and especially following paroxysms of coughing a high degree of distention will occur As we have pointed out when the alveoli are continuously or repeatedly overdistended the alveolar walls become atrophic and the alveoli then remain permanently dilated

In discussing the effect of changes of pressure in the lungs we have not yet taken into consideration the part that may be played by changes in the thoracic cage In patients with emphysema the ribs are elevated and held far apart the costal margins flare the sternum protrudes and the spine is more or less kyphotic The chest is fixed in an inspiratory position and each inspiration beginning from this position must require violent muscular effort to expand the chest sufficiently to take in the required amount of air This is a mechanical disadvantage of great importance Usually it is assumed that the changes in the chest will come gradually as a result of the pulmonary distention but some claim that the bony changes often come first and as they progress and cause an

increased to an enormous degree The lower portion of the chest is held rigidly so that the air is forced chiefly into the upper lobes, and the apices being unsupported by the chest wall or by a heavy layer of muscle, visibly protrude above the clavicles Following violent and prolonged attacks of coughing, the lungs may for a while remain distended, but unless the coughing is frequently repeated they soon return to a normal position We seldom have the opportunity, however to observe the isolated effects of coughing alone There are always complicating factors of equal importance in producing pulmonary distention particularly bronchitis and bronchiolar spasm

Long continued expiratory effort against pressure as is practiced in blowing glass and in playing upon musical wind instruments leads to pulmonary distention which may become permanent but not to emphysema Abundant clinical observation has now shown conclusively that emphysema does not occur more frequently among glass blowers and musicians playing upon wind instruments than among men in other occupations

Fixation of the chest or of parts of the chest during deep breathing leads to pulmonary distention but not to emphysema A study of a large number of men whose daily task is to carry heavy loads upon the back did not reveal a disproportionately large percentage with emphysema

Increased inspiratory pressure alone and increased expiratory pressure alone lead to pulmonary distention only if they are accompanied by hyperpnea The distention so produced may become permanent but the changes in the alveolar walls which are characteristic of emphysema seldom occur It is the effect of combined inspiratory and expiratory increase of pressure in the alveoli that causes the greatest degree of pulmonary distention and if long maintained leads eventually to true or substantive emphysema The effects of obstruction to the free flow of air into and out of the lungs when the obstruction is in the trachea are different from those that occur when it is in the bronchi Tracheal obstruction causes pulmonary distention only when it is of a sufficient degree to cause hyperpnea When the smaller bronchi throughout both lungs are uniformly obstructed—as they are for instance after the injection of histamine—then the same mechanism of respiration obtains as in tracheal obstruction There is no prolongation of expiration, no increase of residual air and no occurrence of pulmonary distention in the absence of hyperpnea We may conclude therefore that any obstruction to the flow of air to and from the lungs that affects all parts of the

tory period is prolonged and a demand for additional oxygen is usually met by an increased volume of respiration with relatively little acceleration of rate The type of response varies greatly however with the degree of emphysema

These mechanical arrangements lead to a great increase of the residual air and a decrease of the complemental air the sum of the two being greater than normal The vital capacity is much reduced The total dead space of the lungs is increased whereas the space through which the inspired air is distributed is reduced Therefore pulmonary ventilation is less complete than it is under normal respiratory conditions and the air less thoroughly mixed The rapid diffusion of carbon dioxide and of oxygen is hindered and the blood is not fully oxygenated The minute volume of inspired air is increased (normal 7+ liters in emphysema average 10+ liters) and after exercise it mounts disproportionately

Investigation of the gas exchange in emphysema demonstrates that the expired air contains more oxygen and less carbon dioxide than it does normally The tension of carbon dioxide in the alveolar air is high (normal 4+ to 6+ per cent in emphysema 6 to 8+ per cent) A patient with emphysema may breathe quietly when the carbon dioxide tension of the alveolar air is at a point which in normal persons would induce very great hyperpnea Scott has studied the response of patients with emphysema to the breathing of air containing varying amounts of carbon dioxide When normal persons breathe air containing 8 per cent of carbon dioxide there is a tremendous increase in pulmonary ventilation the tidal air being increased about 300 per cent Patients with emphysema may breathe a mixture containing 8 to 10 per cent of carbon dioxide with no more than a 25 per cent increase of the tidal air At a somewhat higher concentration however when the pulmonary ventilation is barely doubled distressing symptoms occur marking the limit of respiratory capacity In contrast to healthy persons in whom this limit is reached slowly and with increasingly violent respiratory effort the emphysematous patient suddenly develops severe symptoms as he passes the limit without previously having had any forewarning distress of breathing In a word patients with emphysema have an astonishing tolerance for a high percentage of carbon dioxide in the blood but their range of respiratory capacity is indeed very limited A normal person breathing a minute volume of 7 liters of air may increase his capacity to 50 liters whereas a patient with severe emphysema also breathing while at rest 7 liters of air cannot in any circumstances more than

creased rigidity of the chest the lungs are forced to distend to fill out the enlarged intrathoracic space

Freund[16] was the first to champion this view He describes degenerative changes in the costal cartilages that lead to thickening and lengthening The thickening causes prominence of the cartilages the lengthening a rotation and elevation of the ribs with increase in the size of the chest cavity These changes are found commonly in the aged and often also in early adult life Usually the changes are restricted to the second and third costal cartilages but frequently all the cartilages are involved and the chest increases greatly in size Others have described in addition to changes in the cartilages arthritic changes at the costovertebral articulations which further interfere with the movements of the ribs Still others have emphasized the importance of kyphosis in restricting the excursion of the chest With kyphosis the ribs are elevated the depth of the chest is increased the sternum is forced forward and the lower aperture of the chest is enlarged The extent and location of these alterations will vary with the location of the kyphosis If only the upper dorsal spine is curved the upper part of the chest alone becomes deflated, if the kyphosis is lower the greater part or the whole of the chest may be held permanently in the inspiratory position That these bony changes are factors of importance in the development of emphysema cannot be doubted that they may occasionally be the principal cause of emphysema is possible but that they frequently are the sole cause of emphysema is most unlikely

Pathological Physiology

The position of the chest in emphysema interferes with free ventilation of the lungs When inspiration begins the lungs are already partly dilated and it requires considerable muscular effort to bring in the necessary additional amount of air The muscles of respiration often become greatly hypertrophied The inspiratory act being forcible is quickly accomplished but expiration which is largely passive proceeds slowly and with difficulty In advanced emphysema the expiratory muscles are brought into play Graphic tracings of the respiratory movements show a quick sharp rise during inspiration and a slow gradual fall during expiration The curve of expiration is divided into two phases a short rapid fall followed by a long gradual decline The short rapid fall is due to the immediate elastic recoil of the distended chest Each respira

dyspnea, cyanosis and edema of the dependent parts of the body. These symptoms, very characteristic of myocardial insufficiency and generally thought to indicate heart weakness, may perhaps be explained in another way. It is true that they usually follow an exacerbation of the pulmonary condition, an attack of bronchitis or recurring attacks of asthma, and recede as the pulmonary condition improves. These well established clinical observations were explained, as they reasonably might be, by assuming that the attack of bronchitis or as asthma further impeded the pulmonary circulation and thus added an extra load to the already burdened heart. An entirely different explanation is now offered. The dyspnea and cyanosis are ascribed to the increased oxygen unsaturation of the blood brought about by the greatly augmented difficulty of pulmonary ventilation. The dependent edema is thought to be due to increased peripheral venous pressure and to the effects of anoxemia upon the permeability of the capillary walls.

Our knowledge of variations in pressure in the lesser circulation still is very incomplete. Direct measurements cannot be made in man and they may be obtained experimentally only by procedures that greatly distort normal physiological relations. Most of our information consists of inferences drawn from indirect estimations. It is claimed that there is no interference with the pulmonary blood flow in emphysema, certainly none at least until very late in the disease. The destruction of capillaries, which is such a conspicuous part of the disease, is not sufficient, it is said, to raise the pressure in the pulmonary circulation. The distention of the alveoli favors rather than impedes the flow of blood through the capillaries.

There are factors, however, which increase the pressure in the peripheral venous circulation. Actual measurement of the venous pressure in patients with emphysema often shows a considerable increase. The negative pressure in the chest plays an important part in facilitating the flow of blood from the periphery to the right side of the heart. When the lungs are distended the negative pressure in the pleural cavity is decreased and at the same time the pressure in the veins is increased. It has been suggested, too, that the low position of the diaphragm in emphysema may offer a mechanical impediment to the free flow of blood at the aperture through which the inferior vena cava passes. In this way the volume output of the heart may be decreased. Herbst's[53] observations suggest that there is actually a diminution in the minute volume output. If patients are taught to increase the duration of inspiration and

double or treble this amount Therefore it is easy to understand how very limited in emphysema is the respiratory capacity to accommodate an increased metabolic demand

The tolerance for a high concentration of carbon dioxide in the blood is due to decreased sensitiveness of the respiratory center caused no doubt by the anoxemia The capacity of the blood to store carbon dioxide is thereby increased With a decrease in the oxygen saturation of the blood and an increase in the carbon dioxide tenson, the hydrogen ion concentration is increased provided that the alkali reserve is unaltered In emphysema however, the blood carbonate is greatly increased and this permits a high and fluctuating concentration of carbon dioxide without alteration of the hydrogen ion concentration The oxygen capacity of the blood is usually increased by the polycythemia that is nearly always present The emphysematous patient therefore has in his blood a chemical arrangement which allows him to accommodate to some measure an increased carbon dioxide production but his mechanical factor of safety increased pulmonary ventilation, is very small This mechanism accounts for the delayed oxygen consumption during exercise which increases the oxygen debt that must be repaid Observation shows that during exercise the patient with emphysema uses less oxygen than a normal person but following exercise his oxygen consumption is larger

The marked pack of oxygen in the blood and the polycythemia that is usually present explain the deep cyanosis so conspicuously a symptom of emphysema The degree of cyanosis depends upon the absolute amount of reduced hemoglobin in the blood Therefore the larger the amount of hemoglobin the greater the cyanosis at a given level of oxygen unsaturation

One of the important alterations that occur in the emphysematous lung is the destruction of numerous capillaries in the thin atrophic alveolar walls This decrease in the area of the capillary bed was formerly supposed to raise the pressure in the pulmonary artery, and the heightened pressure to lead to hypertrophy of the right ventricle The idea that emphysema is frequently indeed usually accompanied by right sided enlargement of the heart (cor pulmonale) is firmly fixed in medical thought In recent years, however this seemingly well founded view has been attacked from different quarters Kountz Alexander and Dowell[6] have pointed out that in emphysema the heart is seldom large and that the teleroentgenogram and electrocardiogram do not demonstrate right sided enlargement Many patients with emphysema have

emphysema there is never a noteworthy degree of pulmonary fibrosis, and apparently there are only slight and inconspicuous degrees of sclerosis of the pulmonary arteries

The important part played by bronchitis and bronchial spasm in the production of emphysema has been emphasized This role is so important indeed that it deserves additional emphasis If we except senile emphysema and those rare instances of emphysema due primarily to disease of the bony thorax then we may truthfully say that emphysema is but a sequel to bronchitis and bronchial spasm We have already fully discussed how the obstruction to breathing caused by these two conditions leads to pulmonary distention and the very great importance of the mechanical effects of coughing which always accompanies them in exaggerating the distention Bronchial spasm and bronchitis are almost invariably associated The asthmatic patient after years of attacks coughs even between paroxysms and the patient with chronic bronchitis nearly always has attacks of asthma even though they may be mild The sputum of patients with chronic bronchitis will usually show although it may be transiently a marked eosinophilia Whether bronchitis in addition to the mechanical difficulties it imposes upon respiration also acts deleteriously in other ways is not definitely known It is not unreasonable to assume however that chronic infection may have an effect upon the alveolar walls that decreases their resistance to long continued or oft repeated distention and thus favors the development of permanent dilation of the alveoli and atrophy and rupture of their walls

Pulmonary Emphysema

The effect of positive pressure breathing on respiratory gas exchange has been studied by Motley Lang and Gordon[6] These studies revealed arterial blood demonstrations and expiratory air analyses on 77 patients with emphysema and fibrosis Studies made during ambient and intermittent positive pressure breathing showed a significant rise in arterial oxygen saturation with intermittent positive pressure breathing during which the oxygen partial pressure of the arterial blood was increased—although less markedly in patients without emphysema In 14 of the latter with a transfer gradient of over 20 mm of mercury the alveolar oxygen partial pressure increased from 101 to 111 mm of mercury and the aeration gradient decreased 5 mm of mercury during intermittent positive pressure breathing On the other hand the arterial oxygen

to accelerate expiration by the forcible use of the abdominal muscles the venous pressure falls and the cardiac output is increased It is possible that anoxemia may alter the permeability of the capillary walls and thus facilitate the passage of fluid into the subcutaneous tissues The observations of Krogh and of Landis indicate that an increase of capillary blood pressure occurs with anoxemia

It is also claimed that when the heart actually fails in emphysema then at autopsy both sides of the heart are found to be enlarged Therefore, it is concluded the heart failure is in no measure the result of increased pressure in the lesser circulation but is due to impaired coronary circulation and to the deleterious effects of anoxemia upon the heart muscle

These arguments and demonstrations are persuasive, and easily lead one to believe that the mechanical effects of emphysema upon the heart have been grossly exaggerated And yet it is extremely difficult for one long accustomed to interpret clinical manifestations by these seemingly well founded facts to relinquish at a moment established habits of thought Can it be possible that what has been so persistently taught and readily accepted rests entirely upon erroneous observation The *conclusion is incredible Hamman spoke of this with Dr W B Mac* Callum and at his suggestion Mr H W Jones reviewed some of the cases of emphysema that had come to autopsy It is difficult to tell from the post mortem protocols how severe the emphysema may have been and difficult also from the weight of the heart and the recorded measurement of the thickness of the right and the left ventricles to conclude definitely whether or not the right ventricle had been hypertrophied Minor degrees of hypertrophy easily might be missed In the twenty cases selected however, right sided enlargment was unmistakably present in seven and in four instances in which the lungs and hearts had been preserved hypertrophy of the right ventricle was conspicuous It is possible that the frequency of right sided enlargement of the heart in emphysema has been somewhat exaggerated for it does not always occur Nevertheless these simple observations demonstrate clearly that the association often exists It is interesting therefore to ask what are the special circumstances that lead to right-sided hypertrophy of the heart? To this question there is at present no satisfactory answer It may be that the difference depends wholly or in part upon the degree of emphysema and the length of time it has been present The two well-known conditions that usually lead to pulmonary hypertension are fibrosis of the lungs and arteriosclerosis of the pulmonary arteries In uncomplicated

interpretation Apparently the pressure in the pulmonary artery is often little if any raised and myocardial insufficiency when present may be due to decreased blood flow through the coronary arteries and to anoxemia As we have already pointed out however the edema may be accounted for without necessarily assuming that there is myocardial insufficiency

Cyanosis is nearly always present and may be extreme Osler comments upon the fact that emphysema is the only condition besides congenital heart disease and poisoning with certain drugs in which patients walk about in apparent comfort though they have a startling degree of cyanosis

Some cough is nearly always present and varies from time to time with the degree of asthma and bronchitis Sputum may be absent *or it may be profuse and mucopurulent It is often rich in eosinophiles The amount and the character of the sputum also vary with the bronchitis The symptoms of emphysema therefore depend in large part upon the associated bronchitis It is not uncommon to see patients for many years pass with comfort* through the summer months and become dyspneic blue and wheezy each winter with the onset of bronchitis

The clinical course of emphysema varies with the underlying condition the degree of bronchitis and the cardiac efficiency Many cases last an indefinite number of years and the condition remains almost stationary They have a little dyspnea on exertion but are otherwise comfortable until they contract bronchitis when more marked symptoms come on to subside again as the bronchitis clears In other instances the disease runs a more rapid and uniformly progressive course A bronchial infection fails to clear up cough and expectoration persist dyspnea and cyanosis become more and more marked and bronchopneumonia or cardiac failure terminates the course of events In such instances diffuse bronchiectasis is usually associated with the emphysema In certain cases of pulmonary infection especially tuberculosis a diffuse pulmonary fibrosis often causes marked and occasionally extreme emphysema *The distended lung masks the physical signs of the tuberculosis disease and the underlying condition is unsuspected Repeated and careful sputum examinations often demonstrate tubercle bacilli in the cases of chronic* bronchitis and emphysema that frequent the Outpatient Department of hospitals during the winter months In asthma recurring and long continued pulmonary distention is often followed by structural changes in the lung leading to true emphysema The lungs then remain permanently distended and dyspnea cough sputum and wheezing vary with

partial pressure increased 17 mm of mercury when the transfer gradient decreased 7 mm of mercury—indicating that intermittent positive pressure breathing provided a more uniform alveolar ventilation in these cases In patients without emphysema and with a transfer gradient below 20 mm of mercury similar findings were shown When a significant amount of emphysema was present, however, and the transfer gradient was greater than 20 mm of mercury intermittent positive pressure breathing produced no change in the aeration gradient The alveolar oxygen partial pressure increased 5 mm of mercury during positive pressure breathing and the transfer gradient of 29 mm of mercury decreased 2 mm of mercury Twenty one emphysematous patients had an average residual air of 48 7 per cent of the total lung volume and a transfer gradient of less than 20 mm of mercury In these patients intermittent positive pressure breathing markedly increased the alveolar oxygen partial pressure Thus it would seem that a more uniform alveolar aeration distending alveoli with impaired circulation of air is obtained by intermittent positive pressure breathing and also that arterial oxygen saturation is increased while the mean oxygen gradient of pressure from alveoli to arterial blood is decreased

Maximal breathing capacity is related to the degree of emphysema in a manner similar to the correlation between vital capacity and emphysema Burgess Gordon[51] has stated that if maximal breathing capacity is less than 40 liters per minute emphysema of a significant amount is present

Symptoms

The cardinal symptoms of emphysema are dyspnea, cyanosis and cough Dyspnea is usually the first symptom and also the most constant In the early stages it may be only slight, even on exertion but as the disease progresses, it becomes more and more marked and finally may be extreme even when the patient is at rest The degree of bronchitis that is present has much to do with the intensity of the dyspnea Symptoms often vary in proportion to the bronchitis and bronchial spasm Patients may be comfortable between attacks and very short of breath and cyanotic when bronchitis or asthma develops During the periods of aggravation dependent edema often comes on Heretofore we have ascribed the edema to myocardial failure secondary to increased tension in the pulmonary circulation Recent investigations suggest another

The *roentgenogram* of an emphysematous chest shows the elevated horizontal ribs with wide intercostal spaces The chest seems abnormally long owing to the low position of the diaphragm The heart is usually pulled into a vertical position The lung fields are strikingly clear the hilus shadows wide and deep and the bronchial tree shadows unusually conspicuous Frequently the clear pulmonary fields are marked by shadows cast by old inflammatory lesions These are more common in the upper lobes than elsewhere and probably in many instances represent old tuberculosis foci The lateral roentgenogram is usually of more value than the PA projection since it accentuates the change in the anteroposterior diameter Lateral projection should always be taken where emphysema is suspected

Treatment of Pulmonary Emphysema

Since bronchitis and asthma are the usual forerunners of emphysema the cure of asthma and the prevention of chronic bronchitis would be effective treatment of emphysema Even after the disease is fully developed the prevention of bronchitis if present and its cure will do more to protect and relieve the emphysematous patient than any other measures we can employ The eradication of infection in the upper respiratory passage the avoidance of contact with those having colds and change of climate during the harsh winter months are important

The patient s physical activities should be reduced to a level where symptoms such as cough and shortness of breath may be avoided The patient must learn to live within his limitations

The four important fundamental principles in treating most chronic non tuberculous chest diseases should be borne in mind in the treatment of emphysema The first is to make certain that there is an unobstructed airway Bronchoscopy will eliminate the possibility of the presence of tumors strictures and the effects of external pressure and then we may assume that whatever obstruction to expiration exists must be in the minor air passages and be due to bronchiolar obstruction from spasm and thickening of the air passage walls Frequent use of epinephrine in 1 200 or 1 300 dilution by aerosol suffices to open enough airways temporarily and can be employed for this purpose every two or three hours if necessary The second principle concerns adequate drainage After it is certain that the airway is unobstructed complete inversion of the patient every two or three hours during the day will determine whether the

the intensity of the bronchitis and the degree of bronchial spasm Unless some intercurrent disease carries them off, the patients die of broncho pneumonia or cardiac failure

A congenital form of hyperthrophy of the lungs is described In this condition the lungs are abnormally large, but they show no pathological change and do not produce the usual symptoms of emphysema

Physical Signs

The physical signs of emphysema are very characteristic The chest is full and rounded the anteroposterior diameter much increased and often equal to the transverse The interspaces are wide apart the costal angle is wide, and the costal margins stand out prominently The clavicles also are prominent and the neck appears short from the elevation of the thorax and thick from the hypertrophied respiratory muscles The veins in the neck are full and easily visible As a rule no pulsation is seen over the heart In some instances the dilatation of the thorax occurs only in the upper portion while the lower part remains relatively constricted Some authors would restrict the term barrel-shaped chest to this type Both inspiration and expiration are marked by active participation of the accessory muscles of respiration and although inspiratory efforts may be labored the chest expands but little, the whole thorax being lifted up as a rigid box The expiratory effort is usually much prolonged and when bronchitis is present accompanied by wheezing On palpation fremitus is present but diminished the cardiac impulse is not felt The percussion note is altered Usually it is full and deep and has a drum like quality that is spoken of as hyperresonance The resistance felt by the pleximeter finger is often striking The outline of pulmonary resonance is greatly increased The apical resonance zones are large the area of cardiac flatness is obliterated the lower border of pulmonary resonance extends an interspace or more below the normal limit and the border moves little with inspiration and expiration The breath sounds have a characteristic quality difficult to describe They are distant and faint and instead of being normally crisp and vesicular they are smooth and blowing in quality with somewhat prolonged expiration Moist and sonorous and sibilant *rales* are usually present They vary with the extent of the bronchitis The heart sounds are distant and faint and if many *rales* are present may be inaudible

Bullous Emphysema and Cysts

A type of emphysema characterized by the formation of one or more large cyst like spaces in the lung is termed bullous emphysema William Snow Miller differentiated between bullae and blebs by stating that the pleura is generally intact over a bulla whereas a bleb protrudes like a small bladder on the surface of the lung In either case the two often co exist Certainly bullae may be produced by the conglomeration of distended vesicles within the lung It is justifiable to consider the disease as an entity, since the major physiological disturbance in a given patient may be due to the space occupied by one or more large bullae The disease is much more common in men than in women and especially in men at middle age or past middle age As a rule no antecedent disease can be demonstrated as a factor in the production of the bullae although cases have been known to follow the aspiration of foreign bodies and it has been alleged that irritating inhalants may produce the condition On the other hand bullae are known to be associated with long standing cases of fibroid tuberculosis asthma pneumonoconiosis and chronic pneumonitis

The mechanism involved in the production of bullae must be similar in many cases to that involved in the production of blebs Certainly some bronchial connection must be preserved otherwise the air would be absorbed and the bulla cease to exist Instances of this are recorded in medical literature under the terms pneumatocele pneumocyst and balloon cyst Numerous instances in older age groups have been re corded in the course of routine roentgen examination and as a rule have been found to be of little clinical importance Such patients however are subject to the development of spontaneous pneumothorax or the bullae may become infected leading to abscess formation Occasionally too the bullae may enlarge to such an extent that they occupy the posi tion of an entire lung and these cases may be mistaken for pneumo thoraces

Symptoms

As previously noted there may be no symptoms the disease being picked up by routine roentgenographic examination As a rule if symp toms develop they occur slowly and are those associated with asthmatic bronchitis or chronic bronchitis Dyspnea and cyanosis may develop slowly or be brought about rapidly by intercurrent infection The symptom of substernal oppression is not uncommon

amount of secretion present plays an important part in the production of emphysema The third factor of importance is infection Having cleared the airway and obtained adequate drainage we can be assured that a good deal of infection will take care of itself Generally speaking, antibiotics should be reserved for acute episodes in the long course of emphysema The fourth factor and the most difficult one to deal with is re-education of the patient in the normal mechanics of respiration In these patients the diaphragm is always low and often immobile Since diaphragmatic function contributes about 60 per cent to vital capacity under normal conditions the motion of the diaphragm must be restored Sometimes this can be aided by the use of a belt The use of pneumo peritoneum to aid in the elevation of the diaphragm has also been advo cated but it is not so important as the long continued re education of the patient Most inpatients with emphysema tend to use costal breath ing exclusively They are much more likely however to use abdominal breathing when lying supine and they can be taught to increase the use of the diaphragm by lying with some object of moderate weight on the abdomen and watching it rise and fall as they breathe This mechanism can then be continued when they are erect

Certainly the most important factor in the cure of these patients is long continued observation similar to that employed in the care of tuber culous patients It should extend over a period of years These patients tend to relapse into their old bad habits to neglect themselves and to forget what is taught them

Since smoking in itself tends to produce bronchitis it should be inter dicted Occasionally the use of iodides by thinning the secretions pro duces benefit Aminophylline by month on an empty stomach will sometimes be beneficial since it relaxes the bronchi and permits more efficient respiration Doses of 2 gm in the morning and in the afternoon may be sufficient although larger doses may be given by rectum if it seems to be advisable

Oxygen therapy in severe cases is of great value It may be given through the mouth by nasal catheter in doses of 1 liter for one to two days after which the concentrations may be increased until 5 or 6 liters per minute are inhaled This may be continued for weeks if necessary Intermittent positive pressure breathing as advocated by Gordon[8] and his associates may be used with marked benefit in severe cases

Operation upon the chest wall recommended by some surgeons in the past is mentioned here only to be condemned

(2) The lungs often are prevented from dilating by pressure exerted by pleural effusions by pneumothorax by tumors by areas of consolidation As long as the bronchi remain patent the condition is analogous to physiological atelectasis When the pressure is removed the lungs again expand in a normal way This may be called *pressure atelectasis*

(3) When a portion of the lungs is collapsed and fails to distend after an inspiration is taken which in the circumstances that are present would normally dilate them then there is bronchial obstruction The bronchial obstruction may be the essential cause of the atelectasis or it may occur as it often does when the lung is collapsed from insufficient respiratory effort or from pressure This form of atelectasis may be called *true* or *pathological atelectasis* In general atelectasis develops whenever the blood flows through the lungs and air does not reach them

True atelectasis is the type that interests us clinically It is distinguished from physiological and pressure atelectasis by the fact that there is bronchial obstruction This difference has important consequences as we will soon point out The most important consequence is that pulmonary drainage is interfered with and in this way infection is invited

Physiological Atelectasis In newborn infants the collapsed lungs must be distended by vigorous respiratory movements Weak premature infants often are unable to exert sufficient force to dilate the lungs Cerebral accidents during birth may be the cause of insufficient respiratory movements Artificial respiration often is necessary to start satisfactory ventilation The unequal distention of the lungs that frequently follows is probably caused by bronchial obstruction due to aspirated amniotic fluid or meconium or to the presence of mucus in the bronchi In adults feeble respiratory movements may fail to distend the lungs fully and small areas of collapse may occur at the apices or more commonly at the borders of the lungs A single full breath fills out the collapsed alveoli The filling of the alveoli is usually accompanied by the production of fine sticky *rales* the so called atelectatic *rales* which are frequently heard along the lower border of the lungs

Pressure Atelectasis Compression of the lung causes atelectasis by preventing expansion It occurs in a host of abnormal conditions especially with pleural effusion pneumothorax pericardial effusion increased abdominal pressure et cetera When the pressure is removed the lung re expands If the lung is held compressed for a long time however and inflammatory changes occur it may become fibrous and be unable to re expand even though the cause of the compression is removed

Physical Signs and Roentgen Appearance

In the presence of a large bulla the signs may suggest a localized pneumothorax with hyperresonance and no breath sounds Because of the pressure on the neighboring lung fine *rales* may be heard at the margin of the bulla Moderate-sized bullae are usually multiple, and the roentgenogram is characterized by fine lines of irregularly shaped faintly traced areas in which the normal lung markings are absent As a rule, the lung is everywhere emphysematous and the diaphragm depressed Giant bullae may occupy the area normally occupied by an entire lobe and are often confused with partial pneumothoraces As a rule however, the root shadow is concave only in the area occupied by the bleb and there is no lateral pleural line

Treatment

A life well within the capacity of the patient's physiology is always indicated In addition acute respiratory infections are to be avoided and if they occur immediate bed rest and measures to thin the patient's secretions are advisable for facilitating cough and expectoration If the patient's general condition permits solitary cysts of bullae may be excised surgically

Atelectasis

Atelectasis literally means imperfect extension of stretching Applied to the lungs it designates a condition in which the air cells are collapsed or incompletely filled at a stage of respiration when normally they should be more or less distended For practical reasons it is important to distinguish three types of atelectasis

(1) Only seldom are the lungs fully distended During quiet breathing parts of them do not distend at all If pressure is exerted upon a portion of the chest and movement locally restricted or inhibited the lung beneath is not inflated during inspiration In certain postures when breathing is shallow, large portions of the lung remained collapsed Release of pressure change of posture, and deep breathing at once distend the empty or incompletely filled alveoli This is a normal physiological condition it may be called functional or better perhaps *physiological atelectasis*

lung when the bronchi remain patent—as occurs for instance with pleural effusion and pneumothorax—is seldom accompanied by infection

In addition to the effects of bronchial obstruction upon respiration when large tubes are occluded and the part it plays in facilitating infection there is yet another aspect of bronchial obstruction and atelectasis which gives it pre eminent clinical importance I refer to the fact that atelectasis colors the clinical picture of nearly all pulmonary disease and often usurps the foreground For instance a tumor even though small which presses upon or invades a bronchus may produce a large area of atelectasis and the physical signs caused by the collapsed lung may lead us to infer that extensive pulmonary infiltration has occurred In tuberculosis and in other forms of chronic pulmonary infection bronchial obstruction often occurs Since this obstruction is permanent the collapsed lung usually undergoes fibrosis Instances of extensive pulmonary fibrosis may often be explained in this way especially when they develop quickly and are seemingly the result of tuberculosis Lateral films of the chest in relatively early cases of tuberculosis usually show atelectasis as well as immobile areas in the posterior portion of the upper lobe Undoubtedly these occur as the result of the aspiration of sputum when the patient lies on his back Small bronchial plugs produce the atelectatic areas and thus extend the disease

Atelectatic portions of the lung are contracted and of a deep blue or purplish color They feel soft and pasty and do not crepitate when pressed between the fingers On section they are dry inelastic and non granular If the collapse lasts a long time extensive fibrosis often occurs Postoperative atelectasis is not uncommon and is now frequently recognized The causes of such atelectasis are obvious Respiration is slow because of pain and the use of sedatives while the use of morphine and similar drugs abolishing the cough reflex encourages immobilization and stagnation The dehydration that accompanies many surgical operations thickens the secretions and makes them more likely to produce bronchial obstruction with subsequent atelectasis In addition it has been suggested that traction on the mesentery may produce bronchial spasm

Postoperative atelectasis used to be referred to as postoperative pneumonia It is important to recognize the true nature of the disease since it is the most common postoperative pulmonary complication and can frequently and easily be prevented For obvious reasons upper abdominal operations are more frequently followed by postoperative atelectasis then others Adamson and Dubo[13] report a series of 145 consecutive

True or Pathological Atelectasis The chief cause of atelectasis is bronchial obstruction The area of collapsed lung depends upon the size of the bronchus that is occluded Small areas of atelectasis give no symptoms larger areas may cause severe dyspnea, the plugging of a main bronchus is accompanied by conspicuous symptoms The results of atelectasis may be divided into (a) the mechanical effects upon respiration, and (b) the mechanical effects upon pulmonary drainage

(a) When a large bronchus is suddenly occluded, the patient almost immediately becomes dyspneic, the respirations are rapid and shallow *cyanosis comes on, there is cough usually unproductive, the temperature* rises and a leucocytosis develops The dyspnea cyanosis, and cough are due to the large area of lung which is collapsed the fever and leucocytosis to the infection which quickly occurs If the bronchial occlusion is removed, the atelectasis is not immediately overcome It may be a week or longer before the lung is fully distended

(b) When smaller bronchi are occluded pulmonary ventilation is unimpaired and dyspnea and cyanosis do not occur Nevertheless the occlusion of smaller bronchi producing areas of atelectasis interferes with pulmonary drainage and in this way has important and far-reaching consequences for atelectasis facilitates infection and is often the forerunner of pneumonia, abscess and gangrene When the bronchi are open pulmonary drainage is effectively maintained by the free respiratory movements of the lungs by peristaltic contractions of the bronchi and by the incessant sweeping of the cilia lining the tubes In ordinary circumstances these mechanisms keep the airways clear but should obstacles enter which are not easily removed then the powerful action of coughing is brought into play As long as the bronchial tree is freely open, the lungs have an extraordinary degree of resistance to infection when bronchi are plugged or collapsed infection enters with great ease This is demonstrated constantly by experimental results It is very difficult to produce pneumonia or abscess of the lungs simply by injecting virulent organisms, whereas the attempt is almost uniformly successful if the organisms are introduced in a viscid menstruum or together with solid particles which occlude the bronchi It is a well known clinical observation, which will be more fully discussed later, that pneumonia and abscess are especially likely to occur under circumstances that interfere with deep breathing and therefore lead to insufficient distension of portions of the lungs and at the same time to bronchial obstruction *The determining factor in the occurrence of the infection that often* follows is probably the bronchial obstruction for simple collapse of the

lung when the bronchi remain patent—as occurs for instance with pleural effusion and pneumothorax—is seldom accompanied by infection

In addition to the effects of bronchial obstruction upon respiration when large tubes are occluded and the part it plays in facilitating infection there is yet another aspect of bronchial obstruction and atelectasis which gives it pre eminent clinical importance I refer to the fact that atelectasis colors the clinical picture of nearly all pulmonary disease and often usurps the foreground For instance a tumor even though small which presses upon or invades a bronchus may produce a large area of atelectasis and the physical signs caused by the collapsed lung may lead us to infer that extensive pulmonary infiltration has occurred In tuberculosis and in other forms of chronic pulmonary infection bronchial *obstruction often occurs Since this obstruction is permanent the collapsed* lung usually undergoes fibrosis Instances of extensive pulmonary *fibrosis may often be explained in this way especially when they develop* quickly and are seemingly the result of tuberculosis Lateral films of the chest in relatively early cases of tuberculosis usually show atelectasis as well as immobile areas in the posterior portion of the upper lobe Undoubtedly these occur as the result of the aspiration of sputum when the patient lies on his back Small bronchial plugs produce the atelectatic areas and thus extend the disease

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cholecystectomies in which 16 6 per cent were followed by atelectasis They also note in the same hospital that of 300 consecutive hysterectomies 8 per cent were followed by atelectasis Atelectasis after pulmonary hemorrhage is seen only in the form of massive pulmonary collapse As a rule it is preceded by treatment with morphia or its derivatives, the danger of which has been emphasized under the discussion of hemoptysis Many years ago I had the opportunity of seeing a patient with atelectasis following pulmonary hemorrhage who had been given excessive doses of morphine and had been advised to lie on his affected side exclusively At autopsy the anatomical structure of the lung had almost completely disintegrated The necrotic material could be lifted from the chest as if it were jelly

Symptoms

The sudden occlusion of a large bronchus produces the condition spoken of as *massive pulmonary collapse* The patient immediately becomes dyspneic and cyanotic A little later he has a dry unproductive cough which is sometimes harassing Within twelve hours the temperature begins to mount and remains irregularly elevated for a few days a week or even longer The leucocytes rise and usually vary from ten to twenty thousand After a few days the cough becomes loose and mucopurulent expectoration is raised If pneumonia does not develop and the patient does not die of some other cause the symptoms subside in from five to ten days but atelectasis of portions of the collapsed lung may persist for weeks

Physical examination shows the affected side to be retracted and its respiratory movements greatly diminished or absent The diaphragm is drawn to a high position The percussion note is dull over the collapsed portion of the lung and hyperresonant or tympanitic over the area from which the lung has retracted Vocal fremitus is diminished or absent Usually the breath sounds are greatly diminished in intensity, often they are entirely absent Sometimes they have a tubular quality The voice sounds are transmitted with lessened intensity Only a small number of *rales* or none at all is heard Massive collapse occurs twice as often on the right side as on the left and involves the lower lobe more frequently than the upper or middle The physical signs therefore simulate the signs of consolidation or of pleural effusion When the right lower lobe

is collapsed the very high position of the diaphragm and the elevation of the liver intensify the physical signs of fluid The one characteristic and distinguishing feature is the marked retraction of the mediastinum toward the affected side If the position of the heart is not carefully determined the condition may easily be overlooked but if the heart is found to be dislocated toward the affected side it could be confused only with extensive fibrosis of the lung This error in diagnosis is sometimes made

The roentgenogram is a valuable aid to diagnosis The collapsed portion of the lung casts a dense shadow The lower border of the shadow is usually clear cut the upper border indistinct and mottled The diaphragm is high the intercostal spaces are narrow and the heart and other mediastinal structures are drawn toward the affected side Sometimes the air passages are filled with fluid The shadow of the collapsed lung is then more dense and the diaphragm and mediastinum are not so markedly dislocated

Massive collapse of the lungs occurs only when there is bronchial obstruction Symptoms accompany it when the occlusion comes on suddenly If the bronchus is slowly compressed the symptoms of massive collapse do not develop Although atelectasis cannot occur without bronchial obstruction still there are certain conditions that facilitate the occurrence of bronchial obstruction and these are often the indirect though essential cause of the pulmonary collapse We may divide the causes of atelectasis into (1) primary and (2) secondary The primary cause is bronchial occlusion the secondary causes are insufficient respiratory movements suppression of cough and viscid secretion in the bronchial tubes Pulmonary collapse occurs particularly often in circumstances that bring into play the secondary causes

It would be impossible to enumerate all the conditions under which bronchial obstruction occurs We mention only a few of them The aspiration of foreign bodies that completely occlude a large bronchus causes massive pulmonary collapse An intra bronchial tumor may suddenly plug a large bronchus This occurs not infrequently with pedunculated papillomata that sometimes fall into a bronchus and after a while out again in this way producing repeated attacks of massive pulmonary collapse Massive atelectasis has followed hemoptysis due to a blood clot plugging a bronchus It has been observed to occur after vomiting caused by the aspiration of stomach contents It may complicate pneumonia and other forms of pulmonary inflammation due to

inflammatory exudate lodging in a bronchus It may come on with an attack of asthma and be the cause of death during the paroxysm During the war it frequently followed wounds to the chest It is often observed after surgical operations, especially after operations upon the upper abdomen

Atelectasis may explain the occurrence of pneumonia after exposure in the course of an alcoholic spree after blows to the chest and after submersion It is altogether likely that it accounts for the terminal pneumonia that frequently comes on in patients debilitated by long illness in those exhausted by a chronic infection and in those who remain for a long period in a stuporous condition

In congenital atelectasis the infants are asphyxiated at birth If they are resuscitated by artificial respiration they may live for days or weeks Usually they are feeble and breathing is shallow and rapid The physical signs are those of pneumonia Vigorous infants may recover completely but a number of those who live retain atelectatic areas and subsequently may develop bronchiectasis

Abrams[8] has pointed out that small areas of atelectasis frequently occur in healthy adults These areas are situated along the margins of the lungs (especially at the ends of the clavicles) in the supraspinous fossa, and about the angle of the scapula They give a little dullness on percussion and deep inspiration is accompanied by fine crisp *rales* The signs disappear after one or two deep breaths The condition is important only as a possible source of error in diagnosis

Kronig[98] has described collapse induration' of the right apex which he believes is commonly diagnosed pulmonary tuberculosis The apical resonance zone is contracted there is diminished mobility, the breath sounds are harsh and often blowing and fine *rales* may be heard The condition which I believe to be very uncommon, is said to be associated chiefly with nasal obstruction In contrast to pulmonary tuberculosis there are no constitutional symptoms and the movements of the lower borders of the lungs are normal

Treatment of Atelectasis

The object of treatment is (1) to remove the bronchial obstruction (2) to secure adequate pulmonary ventilation and (3) to prevent infection

The bronchial obstruction is often dislodged by deep breathing and by coughing Frequently it must be removed through the bronchoscope Foreign bodies and tumors are dealt with in this way Plugs of viscid bronchial secretion may require extraction through the bronchoscope by suction or by instrumentation It has been pointed out that in most instances of atelectasis the bronchial obstruction is secondary to insufficient respiratory excursions Removal of the obstruction alone is of only temporary benefit if at the same time satisfactory expansion of the lungs is not induced Often indeed deep breathing alone will dislodge obstructing mucous plugs and also distend the collapsed area of lung When massive atelectasis occurs after operation or in debilitated patients the lungs do not expand after the bronchial obstruction is relieved for days and sometimes for weeks thereafter partial atelectasis persists Therefore only in robust patients is the removal of bronchial obstruction alone curative In the debilitated and in those who are otherwise ill the chief aim of treatment is to obtain adequate expansion of the lungs The principal methods used for this purpose are change of posture and stimulation of breathing by the inhalation of carbon dioxide

Change of posture is a valuable measure to insure uniform distention of the lungs It is a measure that has been practiced for ages Patients who lie constantly upon the back fail to distend the lungs fully and areas of atelectasis develop at the bases of the lungs These are the forerunners of pneumonia usually called hypostatic pneumonia Those who lie continuously upon one side are likely to develop atelectasis in the lung on that side When postoperative massive collapse occurs in patients who are allowed to lie continuously upon one side or are forced to do so by the nature of the operation it nearly always occurs in the dependent lung In these circumstances simply changing the position of the patient so that he lies upon the other side is a valuable therapeutic procedure

The simplest way the most effective way and a perfectly harmless way to induce deep breathing is to allow the patient to breathe mixtures of carbon dioxide with oxygen or with ordinary air This method is now uniformly used in the treatment of carbon monoxide poisoning and in all forms of asphyxia Not only does it help to drive carbon monoxide from the blood but it is equally valuable in preventing the pneumonia that frequently follows It is theoretically and practically the surest and safest treatment for atelectasis Even though the bronchial

obstruction must be removed through the bronchoscope the subsequent inhalation of carbon dioxide at intervals will aid to distend the lung fully and to prevent the formation of the areas of atelectasis that almost uniformly follow The method is also the best way to resuscitate asphyxiated newborn infants An objection has been made to the use of carbon dioxide inhalations upon the theoretical ground that an excess of carbon dioxide in the blood reduces the alkali reserve and shifts the reaction to the acid side There is danger, it is claimed of precipitating a harmful acidosis Henderson[0] has shown that no such danger exists and that the fear springs from erroneous chemical deductions In anoxemia the irritability of the respiratory center is depressed carbon dioxide accumulates in the blood and the bicarbonate or alkali reserve is reduced (acarbia) The inhalation of carbon dioxide not only induces deep breathing but also replenishes the alkali reserve of the blood

The preventon of atelectasis is more important than its cure Frequent change of posture after operation and during prolonged illness has always been advocated especially for debilitated patients The inhalation of a mixture containing 5 to 8 per cent of carbon dioxide with oxygen or with ordinary air is extensively used Scott[101] and others claim that the administration of carbon dioxide for a period at the end of anesthesia greatly reduces the incidence of postoperative atelectasis and pneumonia This claim is contradicted however by the observations of King[95] The treatment may be continued at intervals during convalescence when conditions that favor the development of atelectasis are present It may be that the method will prove equally valuable in medical conditions commonly associated with atelectasis Henderson[91] has reported encouraging observations of its use in the treatment of pneumonia The now generally accepted practice of treating carbon monoxide poisoning the asphyxia of newborn infants and all of other forms of asphyxia with inhalations of carbon dioxide has greatly diminished the occurrence of pneumonia in these conditions In general the treatment of atelectasis is simple and its results dramatic It should not be forgotten however that infection promptly follows the condition and the antibiotics should not be spared once the situation is recognized Certainly if the simplest measures enumerated above are not sufficient to overcome the condition within the first 12 to 24 hours bronchoscopy should be done without further delay since in expert hands this procedure carries practically no risk and is highly efficacious

DISEASES DUE TO FOREIGN BODIES

Pneumoconiosis

Types of Dust

Pneumoconiosis is a condition caused by the accumulation of dust in the lungs Organic dusts are not concerned in the production of pulmonary fibrosis although in some individuals allergic reactions are produced by danders pollens and grain dusts Special conditions such as byssinosis and bagassosis will be considered separately Of the inorganic dusts most are inert producing no fibrous reaction inhaled particles less than 10 microns in diameter may be phagocytosed and carried to the pulmonary lymphatics and hilar lymph nodes After prolonged exposure to large concentrations of these dusts the particles may accumulate in the lymphatics surrounding the pulmonary vessels These deposits may be seen on x ray if the material is radio opaque (siderosis baritosis and so on) Anthracosis the accumulation of carbon particles in the lungs is extremely common occurring in mild degrees in most city dwellers and to an extensive degree in coal miners It is not disabling when found in association with pulmonary fibrosis the latter may be attributed to the silica inhaled with coal dust This condition is designated as anthracosilicosis and the problem is that of a modified silicosis Siderosilicosis also represents the effects of inhalation of iron and silica dust

In contrast to the inert dusts silica excites an excessive production of fibrous tissue Resultant effects will be described in detail since they constitute the major problem of pneumoconiosis Silicates in general are inert but certain fibrous silicates asbestos and talc have been found to produce fibrosis It is possible that further investigations of other industrial processes may reveal hitherto unsuspected forms of pneumoconiosis beryllium poisoning produces a pneumonitis and a delayed form of the disease called granulomatosis Cadmium dusts and fumes produce a pneumonitis but apparently there is no fibrous reaction Exposure to aluminum has been reported to produce pulmonary changes Shaver discovered such changes in workers processing bauxite into corundum The fumes contained both aluminum and silica It remains to be determined which of those is responsible

Silicosis

Silicosis is defined by Gardner[1] as a disease of the lungs caused by breathing air containing uncombined silicon dioxide dust It is characterized anatomically by generalized nodular fibrotic changes throughout both lungs these are demonstrable by x-ray examination and by autopsy and result from any process of occupation involving inhalation of silicon dioxide dust The relation between dusty occupations and pulmonary disability is mentioned in the writings of Hippocrates (460 B C) and Pliny (A D 76) Agricola in 1556 and Paracelsus in 1567 attributed consumption in miners to the inhalation of dust The disease producing cough asthma and consumption among stone cutters was described by Ramazzini in 1705 Zenker in 1867 proposed the term pneumoconiosis' to include conditions resulting from the inhalation of dust of any sort Our present knowledge of the pneumoconioses stems from the intensive investigations since the first decade of this century of various industries by engineers chemists pathologists industrial physicians and clinicians

Silica is the most common constituent of the earth s crust Free silica (SiO_2) in the form of quartz quartzite sandstone flint tripoli chert and opal is the cause of silicosis With the exception of asbestos silicates in which silica exists in a combined form do not cause pneumoconiosis Any occupation concerned with mining tunnel driving or the processing of mineral products may be associated with a silicosis hazard Lanza[139] summarizes the workers so exposed

1 Those who mine in hard (siliceous) rock—gold silver copper lead zinc iron particularly those workers who are engaged in drilling shoveling blasting underground and crushing rock and ore above ground

Those whose occupation is of the nature of mining—workers in tunnels foundations and quarries where the work is carried on in siliceous rock The essential process is similar to mining that is holes are drilled in rock with pneumatic drills the holes are then loaded with dynamite and blasted and the resulting broken rock and debris are shoveled away

3 Those whose work consists of cutting and dressing highly siliceous stone—for instance granite monument workers

4 Those who work in industries where there may be processes that involve exposure to silica dust Such processes are very numerous

indeed and are to be found in glass works pottery works foundries refractory works abrasive works and in grinding and sandblasting

Table I indicates the great number of industrial uses of silica (Ladoo) Sayers[153] and Jones estimate that 1 200 000 individuals in the U S are potentially exposed to a silicosis hazard in the manufacturing and mechanical industries The incidence of the disease however varies considerably in the exposed groups and Cummings[113] estimates that not more than 50 000 employed men might be found in the U S at the present time with definite evidence of this occupational disease

Table I

Industrial Uses of Silica

Uses of Silica	*Types of Silica Used*
Abrasive uses	
In scouring and polishing soaps and powders	Quartz quartzite flint chert sandstone sand tripoli and diatomaceous earth all in finely ground state
In sandpaper	Quartz quartzite flint sandstone and sand coarsely ground and closely sized
In sand blast work	Quartz quartzite sandstone and sand *crushed into sharp angular grains uniform* in size
Metal buffing burnishing and polishing	Ground tripoli and other forms of ground silica
For sawing and polishing marble granite etc	Sharp clean sand graded into various sizes
As whetstones grindstones buhrstones pulpstones oilstones etc	Massive sandstone from very fine to moderately coarse grained
Tube mill lining	Chert flint and quartzite in dense solid blocks
Lithographers graining sand	Medium to fine sand or rather coarsely ground silica and tripoli
Tube mill grinding pebbles	Rounded flint pebbles
In tooth pastes and powders	Various forms of pure silica finely ground
Wood polishing and finishing	All forms of silica ground to medium fineness
Refractory uses	
In making silica fire brick and other refractories	*Fairly pure quartzite known as ganister not* less than 97 per cent SiO_2 nor more than 0.40 per cent alkalies tightly interlocking grains desired

Uses of Silica	Types of S...
Metallurgical uses	
In making silicon ferrosilicon and silicon alloys of other metals such as copper	Moderately pure sand, quartz, sandstone, q...
As a flux in smelting basic ores	Massive quartz and quar...
Foundry mold wash	Ground sandstone, quartz...
Foundry parting sand	Fine sand and ground trip...
Chemical industries	
As a lining for acid towers	Massive quartz or quartz...
As a filtering medium	Massive diatomaceous earth ... finely granular quartz or quartz... ground tripoli diatomaceous ... other forms of silica
In the manufacture of sodium silicate	Pure pulverized quartz sand ... and diatomaceous earth
In the manufacture of carborundum	Pure quartz sand
Paint	
As an inert extender	Finely ground crystalline quartz, ... and flint also finely ground ... sand and tripoli
Mineral fillers	
As a wood filler	Finely ground crystalline quartz, quartz... flint tripoli and other types of ... silica
In fertilizers	
In insecticides	
As a filler in rubber hard rubber pressed and molded goods phonograph records etc	Finely ground silica of all types
In road asphalt surfacing mixtures	
Ceramic uses	
In the pottery industry as an ingredient of bodies and glazes	Flint tripoli chert and other amorphous silica preferred also all other forms of very pure silica all finely ground
In the manufacture of ordinary glass	Pure quartz sand
In the manufacture of fused quartz chemical apparatus such as tubes crucibles dishes	Very pure massive quartz preferred

Uses of Silica	*Types of Silica Used*
Decorative materials	
In the manufacture of gems crystal balls table tops vases statues etc	Rock crystal amethyst rose quartz citrine quartz smoky quartz chrysoprase agate chalcedony opal onyx sardonyx jasper etc
Insulation	
Heat insulation for pipes boilers furnaces kilns etc	*Massive and ground diatomaceous earth*
Sound insulation in walls between *floors etc*	*Massive and ground diatomaceous earth*
Structural materials	
Sand lime brick	*Moderately pure sharp angular sand preferably finer than 20-mesh together with a small percentage of finely pulverized silica*
Optical quartz	
For the manufacture of lenses and accessories for optical apparatus	Clear colorless flawless rock crystal or massive crystallized quartz

Individual Susceptibility The variation in incidence of silicosis where workmen are exposed to comparable concentrations of dust for similar periods of time may be attributed to this factor The upper respiratory passages are ingeniously fashioned to trap dust suspended in the inspired air Abnormalities interfering with this function allow greater numbers of dust particles to enter the lower respiratory tract where some of them succeed in reaching the alveoli Lehman showed that the average retention of silica dust by the nose in non silicotic miners was 50 per cent while in miners with silicosis it was only 2 per cent

Previous pulmonary or bronchial disease seriously interferes with the self cleansing function of the lungs which is dependent upon intact ciliated epithelium adequate production of secretions integrity of the bronchiolar *musculature for peristaltic activity* free access of *phagocytic* cells through alveolar and terminal bronchiolar walls and unimpeded lymphatic drainage Such *conditions* as mouth breathing exposure to other dusts healed pulmonary tuberculosis asthma bronchitis bronchiectasis and bronchiolectasis pleurisy and emphysema interfere with one or several of these functions

Conditions of Exposure. When we exclude the factor of individual susceptibility, the rate of development of silicosis depends upon the concentration of free silica particles in the inspired air and upon the size of these particles. An atmosphere containing 5 million particles of highly siliceous dust per cubic foot is relatively safe. If the silica content of the inspired air is in the neighborhood of 10 per cent, the dust count should not exceed 50 million particles per cubic foot. The maximum permissive concentration of silica in the air breathed might be determined by the percentage of silica multiplied by the total particle dust count. The resultant figure should be less than 5 million.

The most dangerous particles are those 1 to 3 microns in diameter. Those 10 microns in size or larger are less reactive than the smaller particles, settle out more quickly from the air, and are readily trapped by the respiratory defenses before reaching the alveoli. The harmfulness of a given dust depends, therefore, on the number of particles of free silica less than 10 microns in diameter.

Mixture of other dusts with silica reduces the hazard of silicosis by dilution and by causing aggregation and settling. Certain dusts, such as iron oxide and aluminum, appear to impair the reactivity of silica in tissues by coating the silica particles and thereby either reducing their solubility or neutralizing their electrical surface charges.

The time required to develop clinically detectable silicosis varies considerably, depending upon the individual susceptibility and the conditions of exposure. Rapidly developing silicosis has been reported to occur in individuals exposed for one to two years to excessively high concentrations of almost pure silica dust. More commonly the individual has been exposed to the offending industrial dust for five to fifteen years or longer before the characteristic x-ray findings become evident. Even then symptoms and physical findings may be absent.

Pathogenesis. Dust particles under 3 microns in diameter that evade entrapment by the defenses of the upper respiratory tract and reach the alveolar spaces are engulfed by phagocytes. These cells may increase considerably in size as they ingest large numbers of particles; they may lose their ameboid activity and gradually evacuate from the alveoli up to the bronchioles to be expectorated. In general, those dusts that produce the most violent immediate reactions in the alveoli are most readily expelled in this manner. Cells that take up fewer particles migrate through the alveolar walls into the lymphatics and are carried to the regional lymph nodes. In the case of dusts other than silica, a very slight amount of chronic inflammation may develop around clumps

of phagocytes when excessive these cellular collections in the lymphatics and around the pulmonary blood vessels may show as increased density of the pulmonary vascular markings in the roentgenogram

These changes are the same for all non siliceous dusts The response to silica on the other hand is specific The phagocytic cell is destroyed by the silica particles disintegrates and liberates the particles which in turn are ingested by other cells This process continues until each phagocyte contains a sub lethal dose of silica and can migrate to the lymphoid nodules at the junctions of the lymphatic channels Here the irritant action of the silica causes a proliferation of connective tissue in the form of concentrically deposited cells containing collagen The resultant silicotic nodule varies from microscopic size to 2 or 3 mm in diameter The dust laden phagocytes that reach the tracheobronchial lymph nodes excite a similar reaction The smaller lymph channels become blocked by the proliferating connective tissue in the pulmonary lymph nodes With further inhalation of dust the phagocytes no longer able to enter the lymphatic channels remain in the alveolar walls and stimulate fibrotic changes that hamper gaseous exchange between pulmonary capillaries and alveolar air Ordinarily no more than a small fraction of the total number of alveoli undergo such change Thus dyspnea appears only when the disease is well advanced and usually only when infection is superimposed In the so called rapidly developing silicosis alveolar fibrosis occurs relatively early and dyspnea is a prominent feature of the disease The x ray in these cases may not show nodulation since the fibrotic areas are microscopic in size In simple silicosis the nodules may conglomerate especially in areas of previous infection where lymphatic drainage has been impaired Adjacent to the nodules small areas of emphysema appear As a rule the costophrenic angles show no nodulation but become emphysematous Fibrous reaction to subpleural nodules produces a fibrous pleuritis on costal diaphragmatic pericardial and mediastinal surfaces

The mechanism through which silica produces these changes is not adequately explained The mechanical hypothesis which attributes the effects of silica to the hardness and sharpness of the particles has been discarded Such substances as diamond and silicon carbide which are harder than silica produce no fibrosis The solubility hypothesis proposes that silica dissolves in the alkaline body fluids liberating an active sol which poisons the cells Certain observations are at variance with this hypothesis The severity of reaction to various forms of free silica is not proportional to their degree of solubility silicates which

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are more soluble than silica, cause little or no fibrosis, the prompt tissue response to injected silica occurs before much solution can take place and there is no evidence of tissue reactions at points remote from the silica deposits as might be expected if solution had occurred Heffernan proposes that the mode of action is electrochemical in nature that finely divided silica presents a large number of electrochemically active surfaces, while most silicates are arranged in sheets of molecules and are relatively inert

Pathology In non specific pneumoconiosis the pathological changes are due mainly to pigment deposits and cellular collections with little or no fibrosis The degree of fibrosis depends largely upon the amount of free silica mixed with the dust under consideration Grossly such lungs show collections of pigment on the pleural surface that are soft in consistency and are not raised above the surface The cut surface reveals rounded areas of pigmentation with fine deposits of pigment in the interlobular septa and in the walls of the blood vessels Areas of previous infection retain more dust than the rest of the lung On microscopic examination the pigment will be found mainly in the interlobular septa and in the areolar tissue around blood vessels where the lymphatic channels are situated Varying degrees of cellular reaction depending upon the nature of the dust surround the pigmentary deposits

The early silicotic lung may present the picture of perilymphatic pigmentation on gross examination but careful examination may reveal small nodules along the smaller branches of the pulmonary artery The tracheobronchial lymph nodes are at first enlarged but later become contracted hard and on section present a smooth, silky gray or black appearance In the stage of simple nodulation the pleural surface of the lung is studded with nodules 2 or 3 mm in diameter grayish in color and raised slightly above the surface The lungs feel stiffer than normal and firm nodules are palpable throughout their substance At this stage there are no pleural adhesions The cut surface reveals uniformly dispersed discrete gray or black nodules that show little tendency toward conglomeration except in areas of scarring from previous infection Microscopically the nodules consist of concentric whorls of dense hyaline collagenous fibers and occasionally show a central blood vessel Pigment granules may be disposed about the periphery of the nodule and some may collect in the interior The adjacent alveoli contain no exudate but may be dilated More extreme degrees of emphysema occur in advance cases When the inhaled dust contains other minerals in addition to silica as in anthracosilicosis or in siderosilicosis, the

nodules are less uniform in appearance irregular in outline and are connected with adjacent nodules as well as with perilymphatic areas by long fibrous strands

Conglomerate areas of fibrosis may be superimposed upon a background of discrete nodulation These conglomerate areas are composed of large masses of fibrous tissue usually situated in the upper halves of the lungs though occasionally found in the lower thirds They are leathery in consistency black in color sharply circumscribed and present fibrous strands extending into the surrounding parenchyma and to the pleural surfaces Occasionally such conglomerate lesions are seen without a nodular background Although simple silicotic nodules may fuse to form conglomerate masses the presence of these massive areas of fibrosis is generally considered to be due to a combination of infection and silicosis Contraction of the lung and bullous emphysema commonly accompany this type of the disease

Tuberculosis when present may present the usual appearance of chronic ulcerative tuberculosis superimposed upon a background of discrete nodulation This is rare for the usual form of silicotuberculosis resembles massive conglomerate fibrosis the tuberculous process being evident only on microscopic examination There may however be definite gross evidence of infection with areas of caseation and cavitation Fortunately the atypical acute perinodular tuberculosis in which an area of tuberculous pneumonia appears around each nodule with rapid extension of the disease is rare

Diagnosis The diagnosis of silicosis is based upon detailed occupational history symptoms physical findings and x ray examination *The occupational history* should include all occupations since the patient began to work the exact nature of each job and the corresponding dates There should be fairly continuous exposure to silica dust for at least five more often ten years A detailed medical history including tuberculosis contacts should be taken

The classical *symptom* of silicosis is dyspnea the degree varying with the extent of involvement In the absence of complicating infection usually tuberculosis dyspnea does not appear until the pulmonary fibrosis is advanced Orthopnea occurs only when heart failure supervenes *Cough is a frequent symptom usually* paralleling the dyspnea it is dry and nonproductive With infection it becomes more severe and productive and in the later stages is often followed by emesis especially in the morning The sputum varies in character from a thick tenacious mucus to foul purulent secretion It may be blood streaked Hemop

tysis like night sweats, usually indicates an associated tuberculosis

Chest pain is a common symptom and as in most of the dust diseases is usually described as a feeling of tightness in the chest Sharp pain pleural in type may occur In the later stages there is a gradual onset of weakness anorexia insomnia weight loss dizziness and with the onset of cardiac failure edema of the extremities

Physical examination in cases of uncomplicated silicosis usually reveals no abnormalities The subject is usually robust and shows no evidence of impaired pulmonary function In the more advanced cases the findings are those of emphysema with or without evidence of tuberculosis of the lungs There is decreased chest expansion increased tactile fremitus and anteroposterior diameter of the thorax, prolonged expiration impaired resonance with limitation of diaphragmatic motion decrease in breath sounds and inconstant moist *rales* In the presence of complicating tuberculous infection muscle wasting and retraction of the supra and infra-clavicular spaces are present Changes in percussive and auscultatory findings are likely to be more pronounced and asymmetrical with persistent *rales*, and there may be signs of cavitation or of pneumothorax Clubbing of the fingers and curving of the fingernails may be seen in these individuals

In early cases an exercise test and estimation of the vital capacity may indicate reduction in pulmonary function It must be emphasized however that a surprising degree of pneumoconiosis may be revealed by the roentgenogram in the absence of any symptoms or abnormal physical findings Estimation of the erythrocyte sedimentation rate and sputum examinations are to be considered routine in the examination of the silicotic patient Elevation of the sedimentation rate arouses suspicion of a complicating tuberculosis The sputum should be examined for acid fast bacilli by smear concentration methods culture and guinea pig innoculation Where sputum is scant or absent gastric aspirates or tracheal lavage material should be cultured and submitted for guinea pig innoculation

X ray Examination A technically good x ray film is an essential aid in the diagnosis of pneumoconiosis Classification of silicosis is based largely on the roentgenographic findings Sampson groups the changes as follows

A Uncomplicated Silicosis
  N Normal Chest
  P_1 Stage of Peritruncal Exaggeration

P Stage of Marked Peritruncal Exaggeration (pre silicosis)
S_1 First Degree Nodulation (linear markings obliterated and nodules up to 2 mm in diameter present)
S_2 Second Degree Nodulation (nodules to 4 mm in diameter)
S_3 Third Degree Nodulation (nodules over 4 mm)

B Complicated Silicosis
1 Silicosis with Fresh Infection
2 Silicosis with Old Infection
3 Silicosis with Indeterminate Infection

Linear or peritruncal exaggeration is not diagnostic of silicosis nor is it to be interpreted as indicative of fibrosis even when marked It has been described in persons exposed to silica and is presumed to represent an early stage in the development of the disease Deposition of inert pigment right heart failure chronic bronchitis asthma bronchiectasis and the physiological changes incident to advancing age may produce a similar picture

More characteristic of silicosis is the stage of discrete nodulation In the early stages the nodules are small and the normal linear pattern of the lung is still visible As the nodular shadows enlarge to 2 to 3 mm in size they tend to obliterate the linear markings some coalescence of the nodules may appear In the third degree of nodulation there is no trace of the vascular pattern and there is more coalescence of nodules Emphysema is evident in the costophrenic angles The root shadows may enlarge owing to lymph node enlargement and the reaction surrounding the vessels near the hilum may produce a diffuse fibrosis presenting a sunburst appearance at the roots The nodes may later contract and contain foci of calcification The latter may be distributed within the nodes and present the picture of egg shell calcification Enlargement of the cardiac shadow is occasionally present

Conglomerate shadows are presumed to indicate the presence of infection usually tuberculous which may be active or obsolete They are very dense and irregular with sharply defined borders and usually lie in the upper or middle third of the lungs Second and third degree nodulation is usually evident in the surrounding parenchyma though these shadows may be obscured by areas of emphysema Pleural thickening may be present Some observers feel that all conglomerate shadows in silicosis occur only in areas of previous tuberculous infection although it appears that in some cases these lesions may result from nodules drifting together incident to contraction of fibrous bands

Scars of prev . . . . infection may be seen against the background of no . . . . These areas may remain healed and accumulate unusual . . . . in the scar tissue with the result ant appearance of co . . . . icosis already described The tuberculosis may reactiv . . . . by aspiration producing mottled shadows lying betwee . . . . nodules Cavity formation fibrosis and pleural reaction m . . . . Tuberculous reactivation is more likely to cause an atypical . . . . spread designated 'silico tuberculosis This lesion simulates conglo . . . . fibrosis with emphysema and pleural thickening, but over a peri . . . years the shadows increase in size occasionally they break down to form cavities and finally, as though bursting through the confines of its fibrous prison the infection progresses rapidly by direct extension and bronchogenic spread

In addition to reactivation of old tuberculous foci new infections may be superimposed on a silicotic lung These appear as soft mottling usually in the upper portions of the lung The adjacent silicotic nodules lose their sharp borders and become surrounded by a hazy zone Sometimes there is a uniform development involving all of the nodules with the appearance of fluffy shadows around each nodule and extension of these shadows to confluence with the appearance of a tuberculous pneumonia This condition is referred to as perinodular tuberculosis

Treatment Prevention is the key to the problem of silicosis An enormous amount of investigation has gone into the methods of reducing hazardous industrial dust exposure Where adequate measures have been taken to reduce such exposure the results in lowering the incidence of pneumoconiosis have been rewarding Pre-employment examinations are essential to eliminate those individuals who may be abnormally susceptible to the effects of dust Abnormalities of the upper respiratory passages mouth breathing and previous pulmonary and bronchial disease are associated with such predisposition

Once the disease has been acquired in its uncomplicated form most individuals are able to continue at their work provided dust concentrations have been reduced to acceptable levels Periodic examination of such persons often reveals no evidence of progression of the silicosis over a period of many years Should progression occur despite satisfactory working conditions unusual susceptibility may be inferred and further exposure to dust must be discontinued When tuberculosis is suspected the silicotic patient should be removed from contact with siliceous dust both for his own protection and for that of his fellow workers

In 1936 Denny Robson and Irwin[11] demonstrated that finely divided aluminum inhibited the action of silica in experimental animals The early tissue reactions to silica regressed following inhalation of aluminum powder Mature silicotic lesions did not regress but failed to develop further despite inhalation of a mixture of silica and aluminum Inhalation of aluminum dust by silicotic patients resulted in subjective improvement in some but not all individuals Although it has not been demonstrated that metallic aluminum will increase susceptibility to tuberculosis such claims have been made for amorphous hydrated alumina It has been recommended that the general application of aluminum therapy in industrial plants be delayed until carefully controlled experiments show that it is effective in preventing or alleviating silicosis in man It is essential that engineering and medical supervision over dust control be continued with unabated vigilance even when aluminum therapy is employed

Prognosis Simple silicosis is not a disabling disease Disability arises only when there appear unusual degrees of fibrosis and emphysema and in the presence of infection Without exposure to harmful concentrations of dust there is usually little or no progression of the nodular fibrosis It appears that the pessimistic attitude previously held regarding the inevitable progression of silicotic fibrosis is not justifiable at present Following the patient s removal from a dusty occupation some progression of nodular fibrosis may continue until all silicotic particles become encapsulated There is no progression of mature nodules

The outlook in cases of massive conglomerate fibrosis is less favorable Unless the fibrotic areas are small there is usually a considerable degree of emphysema which may in time cause significant reduction in pulmonary reserve A number of these cases may develop pulmonary heart disease with congestive heart failure The latter finding is seen only in extremely advanced cases

Tuberculosis is the most serious complication of silicosis Reports from all over the world from ancient times to the present attest to the frequent combination of these diseases Mortality statistics indicate that the majority of silicotics die with tuberculosis Recent reports are at variance with these figures probably reflecting not only more rigid standards of diagnosis but also the sharp decline in tuberculosis in the general population and the reduced sources of infection Hygienic improvements in industry and in the homes of workers and the weeding

Scars of previous tuberculous infection may be seen against the background of nodular silicosis These areas may remain healed and accumulate unusual amounts of silica in the scar tissue with the resultant appearance of conglomerate silicosis already described The tuberculosis may reactivate and spread by aspiration producing mottled shadows lying between the silicotic nodules Cavity formation fibrosis and pleural reaction may develope Tuberculous reactivation is more likely to cause an atypical form of spread designated silico tuberculosis This lesion simulates conglomerate fibrosis with emphysema and pleural thickening but over a period of years the shadows increase in size occasionally they break down to form cavities and finally as though bursting through the confines of its fibrous prison the infection progresses rapidly by direct extension and bronchogenic spread

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out of infected individuals probably are to a large extent responsible for this reduction which may be expected to continue

Experimental evidence indicates that silica enhances the growth of tubercle bacilli in tissues It has also been shown that silica will reactivate healing tuberculous lesions in guinea pigs On the other hand in silicotuberculosis the infection as a rule progresses very slowly the constitutional signs are few and the recovery of tubercle bacilli is difficult When the host's resistance is lowered however the disease progresses rapidly and presents the familiar picture of advanced tuberculosis The extreme degree of fibrosis in silicotuberculosis may be a factor in restraining the infection and in preventing absorption of its toxic products

When tuberculosis is superimposed on discrete nodular silicosis it behaves similarly to tuberculosis in other individuals and responds in a similar manner to sanatorium treatment As a rule collapse therapy as employed in the usual cases of tuberculosis is not suitable for the inelastic silicotic lung Reports of chemotherapy in silicotuberculosis are not yet available

Primary cancer of the lung does not appear to occur more frequently in silicotics than in the general population The high incidence reported in the Schneeberg and Joachimstal miners is believed to result from the radioactivity of the ores

Prevention Wherever industry has instituted measures to reduce dust counts to safe levels the silicosis hazard has been brought under control The threshold level for silica particles of less than 10 microns has been set at 5 million particles per cubic foot of air Where free silica constitutes only a part of the dust inhaled the total number of particles may be proportionately larger The limits of safety must be determined for each industry

The industrial physician plays an important role in the prevention of the disease Careful pre-employment examination is of great importance In this manner those individuals who may be unduly susceptible to dust diseases can be eliminated X-ray examination of all applicants should be employed to eliminate those with active or healed tuberculosis It may be that tuberculin negative individuals should be given preference for employment in silica hazardous industries Those already employed should also be screened by x ray and tuberculin testing Abnormal x ray findings should be investigated clinically to determine from the nature of the shadows cases of active tuberculosis Those cases discovered to be inactive may be allowed to continue at

work but should be examined periodically for evidence of reactivation Positive tuberculin reactors should also have periodic x ray examinations and the negative reactors should be given periodic tuberculin tests Conversion of the skin test from negative to positive is a signal for careful clinical and x ray examination for clinically significant tuberculosis

Asbestosis

Most of the various silicates that have been investigated have not been found to cause pulmonary fibrosis There are however exceptions the most notable of these is asbestos a hydrated magnesium silicate Exposure to the dust occurs mainly in the manufacture of asbestos cloth Dust counting surveys indicate that the threshold for safe exposure is about 5 million particles per cubic foot The incidence of the disease increases rapidly with increasing exposure

Symptoms do not usually appear before five years of exposure The most prominent symptom is progressively increasing dyspnea with a sensation of tightness in the chest Cough and expectoration are variable In the later stages there is anorexia loss of weight weakness cyanosis clubbing of the fingers and expectoration of tenacious sputum An occasional finding is the asbestos corn a small area of hypertrophy surrounding asbestos fibers embedded in the skin

The early *x ray appearance* is an exaggeration of the linear markings followed by the appearance of a diffuse fibrosis localized in the mid lung fields and in the bases which produces a ground glass appearance When the fibrosis advances there is emphysema in the upper portions of the lung fields pleural thickening pleuropericardial adhesions and nodular and nodulo conglomerate markings The x ray changes may be few in the presence of severe clinical symptoms

Asbestos bodies may be found in the sputum They consist of a core of asbestos fiber surrounded by iron containing protein deposits they are golden yellow in color and stain a brilliant blue with potassium ferrocyanide They vary in size from 10 to 180 microns in length average 35 microns are slender elongated segmented structures with bulbous ends producing dumbell or drumstick shapes Pathological examination reveals these bodies asbestos fibers and phagocytes in the respiratory bronchioles with reticular fibrosis surrounding the bronchioles alveolar ducts alveoli capillaries interlobular septa and pleura Marked emphysema is present in the lungs of those who have died from

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this disease Occasionally there is hyperthrophy of the right ventricular wall There is no evidence that asbestosis is associated with an unusual incidence of tuberculosis

Measures for *prevention* of asbestosis have been adopted with great success These consist of dust control through the use of shields exhaust systems proper ventilation and housekeeping of the working areas use of respirators and pre employment and follow-up examinations of personnel

Tremolite Talc

Another silicate that has been found to cause pulmonary fibrosis is tremolite talc a hydrous magnesium silicate Experimental observations have not demonstrated progressive fibrosis Dreesen[1 3] reported pul monary fibrosis in workers in talc mills and mines and Riddell[151] found fibrosis resembling silicosis in 13 of 37 workers engaged in grinding talc ore Siegal Smith and Greenberg[15] reported fibrosis in 29 9 per cent of workers exposed to talc dust for over ten years Those who had symptoms complained of cough chest pain and excessive fatigue Examination revealed limited chest expansion abnormal lung signs and clubbed fingers dyspnea appeared out of proportion to the extent of x ray findings The x-ray appearance is that of a diffuse, fine haziness and in some cases of nodulation and soft conglomeration Talc plaques —irregular sharply bordered densities—are seen on the pleural surfaces These authors are impressed by the similarity of talc fibrosis and asbestosis

Siderosis

Siderosis is the term applied by Zenker to the accumulation of iron in the lungs The inhalation of iron ore dust alone has not been shown to produce pulmonary fibrosis The hazard for workers in iron mines is most likely attributable to the silica contained in rock which is known to cause siderosilicosis As with other dusts the mixture of iron ore dust with silica diminishes the harmfulness of the latter Siderosis has been reported in hematite miners silver polishers using 'rouge (Fe O_3) as an abrasive foundry grinders and burners metal grinders and boiler scalers

A form of pulmonary infiltration attributed to iron dust is described in cases involving electric arc welders The fumes arising from coated

welding rods in general use consist mainly of particles of iron oxide less than 0 5 microns in diameter and in concentrations of upward of 100 million particles per cubic foot In welders exposed to extremely high concentrations of fumes such as exist when welding is done inside tanks x ray changes have been recorded showing exaggerated trunk markings and in some instances nodular shadows The x ray appearance closely simulates nodular silicosis but these men had no significant exposure to silica They were asymptomatic and examination showed no evidence of functional pulmonary impairment Pathologic examination of the lungs of one individual who died accidentally showed collections of black pigment in lymphatic channels and nodes surrounding blood vessels and bronchi but no scarring Presumably the x ray shadows represent the radio opaque iron dust collections There is no evidence of increased susceptibility to tuberculosis in siderosis

Pulmonary Hemosiderosis

This is a rare non occupational disease Warning signs are increasing pallor lassitude and general debility The pulse is rapid but regular and the chest signs are normal There is a severe hypochromic anemia with leukopenia One characteristic of the x ray is the reticulation of the lung fields consisting of small aggregations about the size seen in miliary tuberculosis in sarcoidosis or following lipiodol installation The densities of reticulation are maximal near the hilar regions and diminished toward the periphery There is no gross nodulation such as is common in the pneumoconiosis group At *autopsy* gross changes are present in the lungs and pleura which show multiple subpleural roughness The pleura is deep purple whereas the cut lung section is rather brown and similar to that of ordinary induration The lung substance is solid and airless The weight of the lung is significantly more than normal The alveoli are crammed with phagocytic cells containing free iron and there are considerable recent interalveolar hemorrhages No obvious deficiencies of the elastic tissue are observed No free iron is present in the spleen liver lymph nodes or reticuloendothelial system It has been postulated that this disease is caused by an unidentified hemolytic agent but modern hematological investigation fails to detect any hemolysins Another postulate is that this condition may be caused by a general breakdown of the alveolar framework The elastic tissue throughout the sections appears to have no abnormalities This condi

tion is also described as being associated with mitral stenosis but it does occur without associated mitral disease *Treatment* consists of administration of blood or packed cells penicillin and oxygen There is a possibility however that this may not prevent an unfavorable outcome

Bagassosis

Organic dusts in general are not concerned in the production of pulmonary disease except in the capacity they may have as allergens Certain dusts such as cotton bagasse and tobacco have been implicated in the causation of pnemonic disease

Bagasse is the product remaining after extraction of sugar from sugar cane The material is baled and used later for manufacture of insulating and acoustic board and refractory brick The cases reported of bagasse disease of the lungs were men engaged in the breaking up of these bales After a variable period of exposure usually three weeks to two months the patients became ill with cough dyspnea and the production of sputum Dyspnea often appeared suddenly and rapidly became severe The sputum was occasionally bloody Cyanosis was rare Rapid loss of weight and weakness were frequently present before the onset of the dyspnea Fever was present in some cases none in others The chest findings were few usually revealing only scattered areas of voice changes and *rales* Roentgenological examination showed bilateral mottling more dense in the hilar regions With recovery complete x ray clearing occurred Examination of tissue obtained by lung puncture revealed spicules of foreign material identified bagasse dust surrounded by a fibroblastic reaction in the interstitial tissues The manner in which bagasse produces the disease has not been determined Fungus and bacterial contamination of the dust mechanical irritation, and allergenic action have been suggested as the mechanism involved but have not been proved

Byssinosis

Byssinosis is a respiratory illness affecting workers who inhale dust in cotton mills The early stage of the disease usually referred to as 'mill fever,' appears to be an allergic manifestation and affects especially workers in the carding room The symptoms consist of irritation of the throat dry cough sneezing conjunctival irritation and occasionally an urticarial rash on the forearms Many workers do not experience mill

fever some have recurrent attacks and others appear to become immune After ten to twenty years of exposure some individuals develop the late stage of the disease There is an insidious onset of weight loss severe cough (dry at first later productive of tenacious sputum) fatiguability dyspnea and a sensation of tightness in the chest The picture is that of chronic bronchitis and emphysema Physical examination reveals marked emphysema X ray findings are consistent with those of chronic bronchitis and emphysema and post mortem examination confirms these findings There is no specific pulmonary fibrosis caused by cotton dust

Berylliosis

Industrial exposure to beryllium compounds occurs in the processing of the ore and in the manufacture of beryllium copper alloy and of fluorescent tubes containing beryllium phosphors

Contact dermatitis may occur after exposure to the acid salts of the metal Cessation of exposure and systematic local treatment will terminate this condition Traumatic deposition of beryllium crystals into the skin results in the formation of a chronic ulcer that heals only when the crystal is removed

Of greater importance than the dermatological effects are the respiratory tract manifestations of beryllium poisoning These occur as nasopharyngitis and tracheobronchitis acute pneumonitis and chronic pulmonary granulomatosis The two former conditions are found in furnace tenders igniting beryllium salts in the production of beryllium oxide or the pure metal By far the most serious manifestation of beryllium poisoning is a pneumonitis characterized by the insidious onset of cough (at first dry later productive of bloody sputum) substernal burning pain progressively increasing dyspnea anorexia and weight loss The temperature is normal or slightly elevated the pulse is elevated *Rales* are heard in both lungs and the vital capacity is reduced Blood counts blood chemistry and erythrocyte sedimentation rates are normal

The duration of the illness is from five weeks to four months X ray examination of the lungs reveals first a diffuse haziness of both lungs followed by the appearance of soft irregular areas of infiltration with prominence of linear markings The soft infiltrations are absorbed later and replaced by a nodular infiltration in both lung fields Clearing occurs in one to four months

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were similar in appearance to those occurring in the skin in cases where beryllium oxide or phosphors had been accidentally introduced

The *course of the disease* is variable In a small series 30 per cent died 30 per cent were unchanged or slightly worse and 40 per cent were improved Beryllium poisoning may be prevented by the establishment of effective measures of fume and dust control in industrial plants the use of protective clothing and masks and pre employment instruction regarding the hazards

DISEASES DUE TO ANIMAL PARASITES

Echinococcus

Echinococcus disease of the lungs is a rare malady in the United States and is discovered almost exclusively in foreigners It occurs frequently in Australia and in Sweden The intestinal parasite *Tenia echinococcus* occurs in dogs and in many wild animals Sheep cattle and swine are the usual intermediate hosts

The infection in man is always contracted from dogs and dogs herding sheep are most frequently infected The *Tenia echinococcus* is a small parasite measuring from 4 to 5 mm in length It consists of three segments the terminal ripe segment containing several hundred eggs When these eggs enter the intestinal canal the embryo is set free and with the aid of its six hooks bores a way through the intestinal wall In most instances it enters the portal circulation and lodges finally in the liver Occasionally it is carried directly to the lung but by exactly what channel is unknown It has been suggested that it may first reach the liver and then the lung by piercing the diaphragm that it may pass through the esophagus and into a branch of the vena cava and thus through the right heart to the lung or that it may pass through the rectum and enter a branch of the inferior hemorrhoidal vein In secondary echinococcus of the lung invasion may occur by extension from a contiguous cyst or by metastasis Most hydatids of the lung are primary and usually when the lungs are infected cysts are not found in other organs

Pathological Anatomy

Echinococcus cysts may be found anywhere in the lung but are most commonly situated in the right lower lobe They may occur at any age but most often between twenty and forty years They vary

In the *treatment* of this condition bed rest is essential until all signs and symptoms have disappeared Administration of oxygen during the stage of dyspnea and cyanosis is beneficial Van Ordstrand[181] reported 5 deaths in 38 cases

Instead of manifesting itself in the acute form just described beryllium poisoning may appear in *subacute or chronic forms* variously referred to as delayed pneumonitis chronic pulmonary granulomatosis or beryllium pneumoconiosis Many of the patients developing this type of the disease were engaged in the manufacture of electric and fluorescent lamps where they handled fluorescent powders containing beryllium phosphors Often the first symptoms appeared many months following cessation of such exposure Dyspnea, cough weight loss anorexia, and occasional fever were the most prominent complaints Examination revealed dullness and moist *rales* in both lungs and occasionally cyanosis Polycythemia was commonly found The blood studies were otherwise essentially normal Vital capacity was reduced Some cases exhibited sarcoid like beryllium granulomata of the skin of the hands

X-ray examination revealed widespread shadows involving both lungs uniformly Where the infiltrate was very fine it imparted a granular or sandpaper' appearance to the film The coarser infiltrates were nodular and less numerous The mediastinal lymph nodes were frequently enlarged as was the cardiac shadow in some cases

Pathologic examination in the acute cases revealed heavy, boggy lungs with extensive consolidation pulmonary edema and moderate enlargement of the bronchopulmonary and peritracheal lymph nodes Microscopically there was a diffuse alveolar exudate composed of large mononuclear cells and edema fluid Lymphocytic and plasma cell infiltration was present in the alveolar walls These changes are in no way different from other types of chemical pneumonitis Even in the early cases however there was evidence of beginning formation of fibrous nodules containing fibrinoid material

In the cases of chronic granulomatosis the lungs grossly were large and emphysematous and contained many small, firm nodules There was thickening of the wall of the right ventricle of the heart and dilatation of this chamber Microscopically there was a progression of the changes found in the acute cases to more pronounced cellular invasion of the alveoli and septa the appearance of emphysematous areas marked fibrosis, and granulomata The granulomata showed a center of fibrinoid material or granular debris and were surrounded by a zone of fibrosis and lymphocyte and plasma cell infiltration These granulomata

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in size from that of a pea to that of a child's head Not infrequently the cysts are multiple

The usual type is the unilocular cyst It may be sterile (acephalocyst) or contain numerous daughter cysts which may develop within the mother cyst (echinococcus hydatidosus endogenus) or between the cyst and the fibrous capsule that walls it off from the lung parenchyma (echinococcus hydatidosus exogenus) The capsule is usually very thin but in long standing cases especially around cysts that have ruptured it may be thick and leathery In the neighborhood of the cyst the lung tissue may be normal but induration often occurs and sometimes abscess and gangrene develop

When the cyst grows to a large size it usually ruptures emptying its contents into a bronchus the pleural cavity, or the lung Occasionally it ruptures into the pericardium into the spinal canal, or through the diaphragm Following rupture the cyst may shrivel up leaving a pasty mass containing lime and cholesterin which is finally replaced by scar tissue More often the cyst becomes infected and a chronic abscess is formed Rupture into the pleura is usually followed by empyema A pyopneumothorax may develop

The cyst contains a clear opalescent fluid rich in sodium chloride and low in specific gravity and in albumin content The characteristic hooklets can be seen microscopically

Multilocular echinococcus cysts seldom occur in the lung

Symptoms and Signs

During the early period while the cyst is still small no symptoms are present Later the patients have cough hemoptysis dyspnea pleurisy and thoracic pain or oppression Sputum is absent or slight unless there is an associated bronchitis The symptoms strongly suggest pulmonary tuberculosis but the patients are usually in good physical condition and there is little or no fever Special emphasis should be put upon hemoptysis which is a constant symptom It is usually small in amount and frequently repeated but occasionally the bleeding is large and a brisk hemorrhage may be the first sympton of pulmonary disease After such a hemorrhage there may be a period of many months or even years before further symptoms appear In the one definite case I have seen a young man in good health had a large hemorrhage After recovery he was well for nearly a year before he entered the hospital again

with profuse hemoptysis On this occasion masses of the cyst membrane were expectorated In the early stage the physical examination may reveal only slightly abnormal signs The side affected may be enlarged and the respiratory movements restricted The percussion note may be resonant dull or flat depending upon the location of the cyst The breath sounds and voice sounds are diminished in intensity In uncomplicated cases there are no *rales*

As the cyst enlarges all of the symptoms especially pain and thoracic oppression become more prominent If the cyst remains intact and does not become infected the symptoms of a large thoracic tumor develop namely bulging of the chest wall dyspnea and displacement of the mediastinal organs Before the cyst reaches such a large size however it usually becomes infected or ruptures If the cyst becomes infected the patient develops fever and the usual symptoms of abscess When rupture occurs in the pleural cavity an empyema forms which may heal completely by drainage or remain open for an indefinite period Not infrequently pneumothorax occurs which may be accompanied by stormy symptoms and be quickly followed by death If the cyst perforates into a bronchus it usually provokes intense coughing and symptoms of suffocation The characteristic cyst contents are expectorated and there is often at the same time profuse hemoptysis After rupture the cyst may collapse and the lesion heal but usually suppuration occurs and a chronic lung abscess results

With the rupture of the cyst very interesting symptoms of intoxication occur similar to the symptoms of protein hypersensitiveness Usually a widespread and intense urticaria is the only hypersensitive symptom but there may be cyanosis dyspnea chills collapse vomiting and convulsions In some instances death has quickly followed the onset of these symptoms

The roentgenogram of echinococcus cyst is very characteristic and is the most important aid to diagnosis A similar picture occurs only in dermoid cysts The shadow is very deep round and absolutely clear cut It looks as though a cannon ball had been placed in the chest This characteristic picture is not always present The borders may be more indefinite when infection has occurred and there are changes in the surrounding lung tissue

The blood usually shows a moderate leucocytosis and a decided eosinophilia sometimes as high as 50 per cent In a certain number of the cases however eosinophilia is absent The blood serum occasionally gives a precipitin reaction with the fluid from a hydatid cyst Of more

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Symptoms and Signs

During the early period while the cyst is still small, no symptoms are present Later the patients have cough hemoptysis, dyspnea pleurisy and thoracic pain or oppression Sputum is absent or slight unless there is an associated bronchitis The symptoms strongly suggest pulmonary tuberculosis but the patients are usually in good physical condition and there is little or no fever Special emphasis should be put upon hemoptysis which is a constant symptom It is usually small in amount and frequently repeated but occasionally the bleeding is large and a brisk hemorrhage may be the first sympton of pulmonary disease After such a hemorrhage there may be a period of many months or even years before further symptoms appear In the one definite case I have seen a young man in good health had a large hemorrhage After recovery he was well for nearly a year before he entered the hospital again

general supporting measures and the use of symptomatic remedies Some cases heal spontaneously after rupture of the sac but the result is always doubtful and the larger proportion of the cases die When an unruptured cyst is favorably located operation offers an excellent chance of recovery Even after the cyst has become infected or has ruptured operation offers a much better chance of recovery than expectant treatment Some patients have been cured by simple puncture but the practice is very dangerous and should not be used

Paragonimiasis

During World War II attention was called to the pulmonary manifestations of paragonimiasis because it is so frequently confused with pulmonary tuberculosis The causative trematode *Paragonimus westermani* is coughed up in sputum passed in feces or released through the ulcerated skin Within a few weeks after reaching water miracidia are hatched which penetrate snails of a number of species The miracidia pass through stages of sporocysts rediae and cercariae The cercariae invade the second intermediate host either crab or crayfish and encyst in the muscles as metacercariae If an infected crab or crayfish is eaten raw or incompletely cooked the metacercariae are freed in the alimentary tract and penetrate the jejunum From the peritoneal cavity the parasites invade the diaphragm and then the lung causing cysts from which more eggs may be obtained In the endemic regions of Africa India Indo China Central China Manchuria the Samoan Islands the Malay Peninsula New Guinea and South America the disease is common Moreover infected dogs cats and other animals have been found in New York Ohio Kentucky South Carolina Mississippi Wisconsin Minnesota and California

Symptoms

In a patient who has eaten fresh water shellfish there is a slowly progressive pulmonary disorder characterized by cough frequent hemoptyses and a thin tenacious watery yellowish white sputum frequently blood flecked Fatigability and chest pain are not uncommon Recently Alvin J Tillman and Harry S Phillips[illegible] observed 12 cases of paragonimiasis in Filipinos on the island of Leyte The patients did not

practical importance is the complement-fixation test using cyst fluid as antigen It is said to be positive in a large proportion of the cases

Diagnosis

The diagnosis of echinococcus cyst is difficult because instances are so rarely encountered If the condition is suspected the history, the physical signs the characteristic roentgenogram the eosinophilia, and the complement fixation test make a satisfactory diagnostic picture In the early stages it is usually confused with tuberculosis The absence of constitutional symptoms and of the usual physical signs of tuberculosis together with the roentgenogram and the blood examination, should clearly separate the two A large echinococcus cyst in the lower lobe may simulate a pleural effusion A careful physical examination should distinguish between the two If it does not the roentgenogram usually will The presence or absence of eosinophilia is another important factor in the differentiation The distinction between echinococcus cyst and tumor may be difficult The presence of eosinophilia and a positive complement fixation test would decide for echinococcus The same factors and the roentgenogram would help to distinguish an infected cyst from an abscess A hydatid cyst of the liver rupturing into the lung may go unrecognized until discovered at operation A correct diagnosis has often been made by examination of the fluid obtained by thoracentesis A clear watery fluid of low specific gravity and containing much salt and only a little albumin is characteristic Hooklets are also frequently found Thoracentesis however should never be done for diagnostic purposes Rupture of the sac nearly always ensues and death frequently follows In suspected cases the Casoni skin test should always be done This is performed by the injection of hydatid fluid into the skin which in the presence of echinococcus cysts may reveal an immediate or a delayed reaction The immediate reaction consists of a weal and erythema which fades away and after the lapse of several hours is followed by an induration and reddening of the skin similar to the reaction obtained in a positive tuberculin test

Treatment

There is no medical treatment for echinococcus disease other than

the diaphragm and invade the lung in a similar way In these circumstances pleural involvement is far more common than pulmonary involvement The pleural or pulmonary symptoms may dominate the clinical picture and the primary growth be unsuspected

TABLE 1

A SUMMATION OF THE INCIDENCE OF PRIMARY CARCINOMA OF THE LUNG A GIVEN BY VARIOUS AUTHORS

Year	Summated from authors who give total autopsies total number of all cancers and total primary lung cancers			Summated from authors who give total number of autopsies and total number of lung cancers			Summated from authors who give total number of all cancers and total number of lung cancers		
	Total autopsies	Total cancers	Total cancers to total autopsies, per cent	Total autopsies	Total lung cancers	Total lung cancers to total autopsies per cent	Total cancers	Total lung cancers	Total lung cancers to total cancers per cent
To 1899	27 126	2201	8 11	63 633	89	0 14	2201	32	1 45
1900–1904	16 323	13 9	8 34	21 818	45	0 21	1614	41	2 54
1905–1909	22 862	2360	10 32	27 268	93	0 35	2595	91	3 50
1910–1914	31 229	3246	10 39	37 580	165	0 44	3560	161	4 52
1915–1919	43 524	4437	10 19	49 244	213	0 43	4857	209	4 30
1920–1924	38,458	4 88	12 47	43 379	354	0 81	5204	344	6 61
1925–1928	6 929	1069	15 43	6 929	94	1 36	1069	94	8 79
1910–1919	74 753	7683	10 27	86 824	378	0 44	8417	370	4 39
1920–1928	45 387	5857	12 90	50 308	448	0 89	6273	438	6 98

Some investigators omit the total number of autopsies others do not give the total number of cancers This incompleteness necessitates the tabular form presented

Of carcinomata that metastasize to the lung breast and kidney tumors are clinically the most important although carcinoma in any organ may cause lung metastases These metastases are frequently small and even though they may be numerous they are usually overlooked clinically Occasionally miliary carcinomatosis of the lungs occurs A lung growth may be the first evidence of recurrence of breast cancer apparently removed successfully years before The association of ob

appear so ill as those with pulmonary tuberculosis although all had the signs of pulmonary disease

Roentgenograms

Positive findings were registered on the first chest x-ray in 11 of the 12 cases reported by Tillman and Phillips [19] In 5 the lesions were small soft and multiple In 6 large areas of density were present The right lung was found to be involved more frequently than the left

Diagnosis

Pulmonary hemorrhage in endemic areas is suggestive of paragonimiasis When this is accompanied by bizarre, multiple lesions shown by x-ray we should seek to establish the final diagnosis by recovery of the ova from the sputum The brownish-red shreds present in the sputum should be carefully searched Although the ova are easily identified unfortunately they are not produced in sputum in quantity, so the search must be persistent The feces and any fluid in the serous cavity should also be investigated Paragonimiasis is not regularly accompanied by eosinophilia

Treatment

Emitin and sulfadiazine in the usual doses have been advised, the latter to combat associated bacterial infection

TUMORS

Carcinoma

Carcinoma is the most common tumor of the lung Secondary growths are observed more frequently than primary ones These secondary growths may occur by direct extension from contiguous carcinomata or as metastases from distant tumors Carcinoma of the breast frequently invades the pleura directly Less commonly it spreads through metastasis to the mediastinal bronchial subclavian and supraclavicular lymph nodes Pleural effusion is usually the first evidence of this invasion Sometimes the growth extends directly to the lung causing little pleural change Carcinoma of the stomach may extend through

and when it does pulmonary atelectasis adds an important element to the clinical picture Histologically the tumors consist of squamous or cylindrical cells in alveolar arrangement In advanced stages both the character of the cells and their arrangement vary especially in the cylin drical cell type

Carcinoma arising from the mucous glands begins in the large bron chi A number of small growths have been described of glandular struc ture with mucoid secretion beginning in the walls of the bronchi and covered by intact bronchial epithelium These typical mucous gland tumors infiltrate the bronchial wall often causing bronchial obstruction As the tumor spreads by direct growth and by metastasis the character istic gross and histological picture may become obscured The secretion of abundant mucus is a very characteristic feature of mucous gland growths although it is not restricted to them

Carcinoma arising from the alveolar epithelium produces infiltrating masses that often spread rapidly involve a lobe or larger area and some what resemble organizing pneumonic consolidation The air cells are filled with epithelial cells cuboidal cylindrical or squamous in type Occasionally the tumors have a papillary structure At times instead of a diffuse growth multiple nodular tumors are formed

All lung cancers produce marked and often early pleural involve ment In late stages numerous metastases occur Occasionally a small lung tumor that gives no local symptoms may cause widespread metas tases Any organ or tissue may harbor metastases but the lymph glands liver brain bones and kidneys are most often invaded In the lungs tumor growth may cause atelectasis cavities bronchiectasis erosion of blood vessels sometimes with fatal hemorrhage and may be accom panied by bronchopneumonia empyema and gangrene

Sarcoma

Secondary sarcoma of the lung is less common than carcinoma but the proportion of sarcomata metastasizing to the lung is greater As in carcinoma multiple tumors that give no symptoms may occur At other times large infiltrating masses are produced Sarcoma of bone and mel anotic sarcoma almost regularly metastasize to the lungs The sec ondary tumors do not always faithfully reproduce the structure of the primary growth

Primary sarcoma of the lung is rare probably even rarer than reports

scure or unusual pulmonary symptoms and signs with one or more nodules in the bones is peculiarly characteristic of hypernephroma The presence of this tumor is sometimes predicted from these remote manifestations before there is any local evidence of a renal growth

Primary carcinoma of the lung is no longer an uncommon disease During the past thirty years it has been detected with steadily increasing frequency Rosahn has collected a large number of reports and the table that summarizes them is here reproduced

We can see that the incidence of all forms of cancer discovered at post-mortem has increased from 8 per cent to 12 + per cent during the past thirty years and that cancer of the lungs has advanced from 0 2 per cent to 0 9 per cent Opinions differ about the cause of this increase Some believe it is only a reflection of the lengthened span of life and of improved diagnosis They point out that since more people live to be fifty years of age or over more die of the diseases of late life, among which cancer occupies a prominent place They also contend that physicians are now more alert to suspect lung cancer and better equipped to diagnose it Others contend that the increase is too large to be accounted for in this way alone and point to the fact that the increase of pulmonary cancer is greater than the increase of all of other forms of cancer We have not yet sufficient data with which to settle the dispute although opinion seems to incline to the view that an actual increase has occurred It is interesting to note however that two authors Rosahn [0] and Fried [189] using the same statistical material arrive at opposite conclusions Rosahn writes the post mortem incidence of primary carcinoma of the lung is steadily increasing and this increase is real and absolute while Fried states the increase is very likely more apparent than real' Whatever the truth of the matter may be the fact remains that physicians now recognize carcinoma of the lung much oftener than they formerly did and that it has become an increasingly important problem in pulmonary diagnosis

From the histogenetic standpoint three types of pulmonary carcinoma are recognized arising respectively from the bronchial epithelium, the bronchial mucous glands and the alveolar epithelium

Carcinomata arising from the bronchial epithelium often cause bronchial obstruction and bronchiectatic cavities, they seldom cause a diffuse tumor of the lung When the growth has reached large size it often forms a mass at the hilus of the lung surrounding the large bronchi with projections along dilated bronchi which form large bronchiectatic cavities in the mass of cancer tissue Bronchial occlusion usually occurs,

and when it does pulmonary atelectasis adds an important element to the clinical picture Histologically the tumors consist of squamous or cylindrical cells in alveolar arrangement In advanced stages both the character of the cells and their arrangement vary especially in the cylindrical cell type

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lead us to believe because many tumors reported as sarcoma have been insufficiently studied Certain inflammatory changes in the lungs may simulate sarcoma in structure and certain areas of carcinomata are indistinguishable from sarcoma Pulmonary lymphosarcomata must always be secondary to tumors arising in lymph glands or in the thymus The diffuse spindle celled tumor is the most characteristic and the most common of lung sarcomata It usually causes a large infiltrating mass, but there may be smaller multiple tumors Peribronchial sarcomata are described which presumably arise from the bronchial walls They are made up of small round cells and resemble lymphosarcoma and since the bronchial glands are always involved, they may be extensions of gland tumors It is difficult to distinguish these growths from a certain type of carcinoma Large round cell tumors similar to the spindle cell growths are described

Symptoms

The symptoms of carcinoma of the lung are no different from those of other pulmonary affections They often differ however in quality, in intensity and in their combinations The chief symptoms are cough pain dyspnea and hemoptysis Cough is almost always present and is usually the first symptom Since most lung cancers are bronchiogenic cough in the beginning is usually due to bronchial irritation or obstruction The cough is a dry irritative cough often occurring in paroxysms and sometimes in paroxysms of great severity It may be accompanied by a wheeze or stridor Less often the cough is nothing more than a frequent hack which may be disregarded by the patient or ascribed to smoking No sputum but a small amount of frothy serous expectoration is raised Mucopurulent sputum comes at later stages when infection of the surrounding lung tissue occurs or the tumor becomes necrotic

Pain is usually complained of often as the cough begins and sometimes even before there is cough The pain is different from the pain of pulmonary inflammation In inflammation pain is due for the most part to pleural involvement but in cancer pain may be present long before the pleura is affected It is a deep dull constant pain without the respiratory accentuation of pleurisy At later stages pain may be due to pleural involvement to pressure upon nerves or to bone metastases

Dyspnea is the conspicuous symptom of lung cancer At an early stage it is out of proportion to the extent of pulmonary involvement Patients may complain of difficulty in breathing at a time when the

physical examination of the chest reveals no abnormality and the roentgen ray shows but slight changes in the lungs Later dyspnea is increased by bronchial obstruction extensive pulmonary infiltration and pleural effusion

Hemoptysis occurs frequently with cancer of the lung but in early stages it is usually slight often no more than streaking of the sputum Later small hemoptyses of from o to 50 cubic cm are common Large hemorrhages may occur sometimes fatally but they are rare Small frequently repeated bleeding is more characteristic of carcinoma than a single large hemorrhage

Anemia loss of weight and weakness come at late stages of the diseases A great variety of symptoms is caused by infiltration of neighboring structures and by metastases Hoarseness is common owing to pressure upon the recurrent laryngeal nerve Dilation of superficial veins indicates pressure upon the mediastinal veins difficulty in swallowing pressure upon the esophagus inequality of the pupils and enophthalmos pressure upon the cervical sympathetic ganglia Involvement of the heart may be accompanied by the symptoms of myocardial insufficiency Clubbing of the fingers now and again and occasionally a striking degree of pulmonary osteoarthropathy is observed

Fever deserves to be mentioned because of its importance in diagnosis It is always present at late stages of the disease and sometimes at earlier stages as well At early stages it is usually inconspicuous not over 100 F or thereabout at late stages it is often much higher The presence of fever frequently dissuades physicians from considering the possibility of carcinoma

Physical Signs

There is nothing peculiar about the physical signs of lung cancer although a certain combination of signs may be suggestive A deep seated tumor may give no signs whatsoever An infiltrating mass may give the signs of pulmonary consolidation Pleural effusion frequently occurs and when it is present obscures the recognition of what may be in the lungs beneath It is well to remember that at late stages of pulmonary cancer the symptoms and signs that may be present are due more to the changes in the lung caused by secondary infection and bronchial obstruction than to those caused by the growth itself Nevertheless certain combinations of physical signs may suggest a tumor of the lungs Retraction and immobility of the affected side are more pro

nounced than in other pulmonary diseases In inflammatory lesions exudation into the lung leaves the bronchi patent

The physical signs of such consolidation are dullness, tubular breathing bronchophony and usually moist *rales* Carcinoma invades all structures in its path closing off the bronchi as it proceeds The physical signs of such consolidation are marked dullness diminished intensity of breath sounds and voice sounds and usually few or no *rales* These statements are in a way schematic for in practice many exceptions to them occur

Diagnosis

In considering the diagnosis of pulmonary carcinoma we may divide its clinical manifestations into three groups

1 Instances in which the lung growth is secondary to a primary cancer located elsewhere

2 Instances in which the primary growth is in the lung, but the first clinical evidence of its presence comes from metastases to distant organs

3 Instances in which the primary growth is in the lung and the earliest symptoms come from its presence there

1 Secondary lung metastases Secondary metastatic carcinoma of the lung is more common than primary carcinoma In most instances it is easy to diagnose Pulmonary metastases may occur (a) as small circumscribed nodules (b) as larger areas of infiltration, (c) as miliary nodules scattered diffusely throughout the whole or part of the lung or (d) as pleural lesions Metastases may come from a primary growth situated anywhere in the body Often they are merely a part of late generalized metastasis and have no clinical importance Less frequently they occur as localized metastases, and if the site of the carcinoma from which they come is obscure they may be mistaken for primary lung growths or for some other pulmonary disease Sometimes even though it is known that a carcinoma situated elsewhere has previously been removed the occurrence years after of an isolated pulmonary metastasis may be very difficult to diagnose Although pulmonary metastases may come from unrecognized carcinoma located anywhere or may follow the removal of any cancer nevertheless they occur especially often with tumors of the breast, kidneys and thyroid gland

The clinical manifestations are variable At times there are no pul

monary symptoms and the lesions are revealed often unexpectedly by the roentgen ray At other times the patients have cough fever and pain in the chest Physical and roentgen ray examinations may reveal a localized area of infiltration in the lung and the whole clinical picture may for a time be indistinguishable from pulmonary tuberculosis At still other times the patients have cough dyspnea and more or less marked constitutional symptoms The physical examination of the lungs may reveal little that is abnormal but the roentgenogram may show scattered miliary lesions suggesting miliary tuberculosis or a fungus infection Finally many patients complain only of increasing shortness of breath and examination reveals a pleural effusion Again and again in these circumstances tuberculosis of the pleura is mistakenly diagnosed

To this group of metastatic lesions we may add the instances of direct extension to the lungs from contiguous growths Carcinoma of the esophagus often invades the lung simulating the clinical picture of lung abscess Carcinoma of the stomach may penetrate the diaphragm and attack the lungs

4 *Unsuspected lung tumors revealing themselves first through distant metastases* Frequently metastases produce conspicuous symptoms whereas the primary growth causes none or only comparatively slight ones, and therefore escapes notice Even when diligently sought it may not be discovered Carcinoma of the lungs often appears first as a tumor of the brain of the bones or of the liver The lung cancer may be entirely overlooked and found unexpectedly at autopsy The occurrence of brain metastases with carcinoma of the lungs is especially frequent—so frequent that it has become routine custom carefully to search the lungs of every patient with brain tumor This association has been particularly emphasized in reports from the Peter Bent Brigham Hospital at Boston There they find that over 30 per cent of lung cancers have cerebral metastases This astonishing figure cannot be accepted as a generally applicable proportion for the conditions at that hospital are unusual *Owing to the large number of patients with brain tumor* brought there for operation the association with cancer of the lung is *unduly exaggerated* Nevertheless *experience demonstrates that the two often go together and that the symptoms of brain tumor may precede for months and even for years the symptoms of the primary growth* in the lungs

In other instances severe pain due to bone metastases may be the earliest symptom of a lung cancer In still other instances an enlarged

nodular liver may direct suspicion to the gastrointestinal tract, causing the lung growth to be overlooked

It is interesting to note the frequency with which metastases from pulmonary carcinoma involve the different organs Illustrative figures are taken from autopsy protocols and therefore record the conditions present at death when wide dissemination has usually occurred It would be more helpful clinically to know the frequency with which the different organs are the first to be reached by metastases but about this we have no information The following table is compiled from the records published by Simpson [05] Rogers [201] and Kikuth [195]

FREQUENCY OF METASTASES TO DIFFERENT ORGANS FROM LUNG CANCER

	Simpson 139 cases	*Rogers 50 cases*	*Kikuth 240 cases*	*Totals*
Regional glands	104	39		143
Lungs	16	14		30
Pleura	31	10		41
Bones	85	19	48	152
Liver	45	17	70	132
Extrathoracic glands	70	11		81
Suprarenals	41	17	21	79
Brain	19	10	31	60
Kidneys	14	11	25	50
Pancreas	25		11	36
Heart		11	4	15
Thyroid	4	4	5	13
Intestines	8	1	3	12
Spleen	5	2	2	9
Stomach	2	2	2	6

3 *Primary carcinoma of the lungs* Primary carcinoma of the lungs manifests itself clinically (a) as bronchial irritation or compression, (b) as a well circumscribed tumor, (c) as infiltrative pulmonary disease (d) as pleurisy usually with effusion and (e) as a disseminated miliary infiltration

Cancer that arises in a large bronchus usually causes first an irritative paroxysmal often stridulous cough Pulmonary signs may be entirely absent until bronchial compression or occlusion occurs Then there may be suppression of breath signs later the manifestations of atelectasis and finally the clinical picture of bronchiectasis or abscess Often these tumors are earliest diagnosed with the aid of the bronchoscope They

may simulate mediastinal tumors tuberculosis and syphilis and later in the course of the disease, bronchiectasis and abscess

Cancer of the lung occurring as a circumscribed tumor usually arises at the hylum and gradually extends into the lung substance When plainly visible on the roentgenogram it may be a later stage of the bronchial tumor causing first bronchial irritation and then obstruction A harsh irritative paroxysmal cough is the chief symptom usually accompanied by pain This cancer may be mistaken for mediastinal tumors for benign tumors and later for tuberculosis or abscess

Cancer occurring as an infiltrating pulmonary disease usually begins in the parenchyma of the lungs arising from smaller bronchi or from the alveolar epithelium The symptoms are frequently those of a chronic pulmonary infection i e, fever cough prostration This type of lung cancer is often mistaken for tuberculosis bronchopneumonia chronic nontuberculous pulmonary infections and fungus infections It gives no characteristic roentgen ray picture and usually escapes detection through the bronchoscope

The pleurae may be the seat of primary cancer but far more commonly they are secondarily involved by metastases or by direct extension Often when the patient first consults a physician, complaining of pain and shortness of breath a pleural effusion is discovered It is then often impossible to tell by physical or roentgen ray examination what is the condition of the lung beneath Absence of fever an insidious onset severe pain and disproportionate shortness of breath may arouse suspicion but at first the disease is usually diagnosed tuberculosis To distinguish between the two is extraordinarily difficult

Primary carcinoma of the lung occasionally occurs as a diffuse miliary infiltration This form of the disease has attracted great interest and the literature on the subject has been collected by J Wolff The patient usually becomes ill with the symptoms of a pulmonary infection The physical signs are indefinite The roentgenogram shows a miliary infiltration resembling the mottling of miliary tuberculosis or of a fungus infection The constitutional symptoms are marked and the disease runs a rapid course

Differential Diagnosis

Carcinoma may simulate any other disease of the lungs and to distinguish between them is often difficult The early symptoms may suggest a mediastinal tumor When the lung is invaded tuberculosis fungus

infection, syphilis and bronchopneumonia may be imitated When abscess, bronchiectasis or empyema occurs, these complications may be attributed to other causes

If bronchial obstruction is the earliest symptom, compression from a mediastinal tumor must be considered Aneurysm, lymphosarcoma, Hodgkin's disease secondary carcinoma of the mediastinal glands, and benign growths must be excluded At later stages stridor, paralysis of the recurrent laryngeal nerves, and Horner's syndrome may still more strongly suggest a mediastinal growth Hodgkin's disease may at times cause but little enlargement of the mediastinal glands and produce pleural effusion or a curious pulmonary infiltration that resembles carcinoma

Tuberculosis is the most common chronic infection of the lung and is more often confused with carcinoma than any other disease When the first symptom of carcinoma is a pleural effusion, the distinction between the two is particularly difficult, as has already been pointed out When the carcinoma infiltrates the lung it may closely simulate pulmonary tuberculosis In both there may be fever, cough and sputum wasting and the signs of consolidation Usually there is more fever and less pain in tuberculosis Absence of *rales* is in favor of carcinoma In advancing tuberculosis tubercle bacilli are seldom absent from the sputum on repeated examination

Fungus infection of the lung fortunately is a rare disease in this country The occasional instances that come to our notice, however particularly infections with streptothrix and actinomycosis may resemble carcinoma

Syphilis too, is a rare disease of the lung Occasionally it may have the appearance of carcinoma

The clinical manifestations of carcinoma often begin and proceed with symptoms suggesting a mild bronchopneumonia or localized pulmonary infection I recall a number of patients who stated that their illness began acutely with a cold followed by bronchopneumonia that had not resolved Undoubtedly in most of these patients less prominent symptoms must have occurred before the more conspicuous ones came on The patients ignored them however or else they forgot them remembering only the serious manifestations

Pulmonary suppuration occurs frequently at late stages of carcinoma, and often the symptoms of suppuration usurp the foreground of the clinical picture and carcinoma is unsuspected Pulmonary abscess or

empyema may be diagnosed and carcinoma be discovered only at autopsy

While the *roentgen ray* lends valuable aid to the diagnosis of carcinoma of the lung its value in primary tumors is not nearly so great as one would anticipate Secondary growths are usually portrayed as multiple sharply outlined shadows that have a characteristic appearance Their presence can often be diagnosed from the roentgenogram when symptoms and physical signs are absent Pleural effusion of course obscures the affected side by a dense shadow that makes it impossible to discern the condition of the lung beneath When the tumor is intrapulmonary the shadows are by no means characteristic and are often misleading Even when a diagnosis of lung tumor may be made from the other clinical evidence the roentgenologist will often report pulmonary tuberculosis unresolved pneumonia localized pleural effusion or nontuberculous infiltration I have seen instances of such disagreement in which the subsequent course proved the clinical impression to be correct In a number of other instances in which the symptoms of a beginning tumor were misinterpreted the roentgen ray lent full approval to the misinterpretation I cite these experiences not to belittle the value of roentgen ray in the diagnosis of lung growths but to warn physicians against too implicit reliance upon the roentgen ray definitely to verify or disprove the presence of a tumor

Treatment

There is no treatment for carcinoma of the lungs other than surgical treatment Lobectomies and pneumonectomies are now being performed at many medical centers and often with astonishing success Surgeons stand ready to attempt the removal of lung cancer if physicians will send them reasonably early cases Therefore the successful treatment of carcinoma of the lungs now depends upon early diagnosis

The symptoms at an early stage must be almost negligible and unless the physician is suspicious of even trifling symptoms and keen to follow up the suspicion with persistent investigation an early diagnosis will never be made There is good ground for the belief that the duration of life after the beginning of carcinoma of the lung is much longer than we are accustomed to judge If we estimate the duration of life from the time at which patients date their earliest symptoms then the duration averages from six months to two years There are however instances

recorded of patients living from five to seven years after the tumor had been recognized The conditions seem to resemble those of carcinoma of the stomach Often symptoms appear only when the growth has already reached a large size

If we are ever to make an early diagnosis of cancer of the lung our attention must be focused upon slight symptoms Suspicion should be easily aroused and once it is aroused careful investigation may now and again be rewarded A cough no matter how trivial, in a person over forty years of age should be suspected If the cough persists and especially if it is a dry irritative cough and still more especially if it occurs in paroxysms the suspicion is strongly confirmed If in addition to this there is pain then we are justified in making a presumptive diagnosis of carcinoma The bronchoscope and the roentgen ray will be our most valuable aids to further investigation The physical examination will be less helpful but in making the physical examination we must be attentive to the slightest alterations An area of diminished breath sounds may be very suggestive When grossly abnormal physical signs are present the tumor is usually beyond the successful reach of surgery

When we consider the location of tumors of the lung, the long periods during which they may give no symptoms, and their inaccessibility to our methods of examination then we must realize that it is vain to hope that we shall detect them all at an early stage When they are recognized most of them will no longer be operable Nevertheless if we succeed only occasionally in making an early diagnosis, our efforts will be sufficiently rewarded

Benign Tumors

Benign tumors of the lungs, excepting dermoid cysts have little clinical interest They seldom give symptoms and are discovered accidentally upon roentgen ray examination or at autopsy Fibromata lipomata and osteomata occur

Dermoid cysts rarely occur in the lung, usually they begin in the upper anterior mediastinum and involve the lung by compression or by rupturing into it They vary in size from tumors as big as a walnut, discovered accidentally at autopsy to masses as large as a child s head containing as much as three liters of fluid The walls are usually thin but densely adherent The cysts almost regularly contain hair, and in the walls bone cartilage teeth glands, and other structures are commonly

found In about half of the cases the cyst ruptures into a bronchus Less commonly it ruptures into the pleural cavity, the pericardial cavity the lung the aorta the vena cava and externally through the skin

The symptoms are extremely varied They usually begin after puberty over 50 per cent of the cases producing the first symptoms between the twentieth and thirtieth years Sometimes the mediastinal mass is discovered before symptoms occur at other times when the first symptoms are associated with rupture of the cyst grave manifestations may suddenly appear The chief symptoms that occur are dyspnea pain pleural effusion cough and sputum Recurring hemoptysis is common When the cyst ruptures into a bronchus sputum is usually abundant In from one quarter to one third of the cases hair is found at some time in the sputum Horny epithelial cells fat droplets and cholesterin crystals may be found in the sputum and give the clue to the correct diagnosis After symptoms appear the disease usually progresses rapidly and death occurs in from four to five years Sometimes death occurs very quickly after the symptoms of rupture appear at other times symptoms last for many years in one instance for 44 years The physical signs are those usually associated with mediastinal tumor When the cyst is very large and particularly when it is situated in the posterior mediastinum it may simulate a pleural effusion After rupture has occurred the signs may be very confusing and lead to great difficulty in diagnosis

Dermoid cysts may be distinguished from malignant disease by the age incidence the longer duration of symptoms and the absence of cachexia Pressure symptoms are less common with dermoid cysts than with malignant growth or aneurysm It is often difficult to distinguish it from pleurisy with effusion encapsulated empyema and abscess

The only treatment is surgical Many cases have been operated upon with benefit The usual procedure is to incise and drain the cyst The whole tumor has been successfully removed

Pulmonary Hamartomas These tumors are said to arise in aberrant anlagen and contain some or all of the normal histological elements found in bronchi or lung tissue These elements however are quantitatively grouped in abnormal proportions so that one tissue usually cartilege predominates Probably some of the reported chondromas of the lungs were actually hamartomas Usually these tumors are firm having the consistancy of cartilage and are rounded or lobulated in outline They may be found when minute or may grow to huge masses that fill one side of the chest For the most part they are benign although

malignant degeneration has occurred Most of the recorded cases have been asymptomatic and discovered by routine x-ray Since the tendency now is to remove all questionable masses appearing in x ray films, the diagnosis has become more frequent It is doubtful, however if removal of small hamartomas is necessary If calcification and ossification appear on the x ray and it is felt that hamartoma is the likely diagnosis, delay may be justified

INFLAMMATORY DISEASES

Bronchopneumonia

The terms bronchopneumonia lobular pneumonia and catarrhal pneumonia which are used synonymously are employed to distinguish certain types of pulmonary inflammation from a nearly related form of pulmonary inflammation designated lobar or croupous pneumonia (for discussion of lobar pneumonia see chap XXVIII in vol IV) There are excellent reasons for wishing to make this distinction from both an anatomical and a clinical standpoint but the terms proposed do not embrace these reasons Catarrhal pneumonia is an obsolete term, fortunately now little used it refers to the association of areas of consolidation with bronchial catarrh Lobular pneumonia is a purely anatomical concept, indicating an important but not a constant distinguishing feature Bronchopneumonia emphasizes the important role of bronchial inflammation and the spread of the infection from the bronchi to the surrounding alveoli All of these terms are unsatisfactory because bronchopneumonia is not always secondary to bronchitis or bronchial catarrh, it is not always lobular in arrangement, and the really important reason for distinguishing lobar and bronchopneumonia is not even suggested This important reason is the difference in the clinical course of the two diseases Lobar pneumonia is essentially a primary disease, bronchopneumonia is essentially a secondary disease, lobar pneumonia has a characteristic clinical course bronchopneumonia has a protean clinical course lobar pneumonia has a uniform pathological picture bronchopneumonia has a varied pathological picture, lobar pneumonia is due to a definite and constant bacterium, bronchopneumonia is due to many different organisms In a word lobar pneumonia has as its distinguishing mark the characteristics of a specific infectious disease Bronchopneumonia lacks these characteristics entirely Unfortunately many exceptions occur to these generally valid statements Certain cases of primary

bronchopneumonia clinically resemble the classical picture of lobar pneumonia and certain instances of lobar pneumonia are indistinguishable clinically from bronchopneumonia While most cases of lobar pneumonia are due to the pneumococcus other organisms may cause lobar consolidation The specific bacterium of lobar pneumonia is also the most frequently found organism in secondary bronchopneumonia There is therefore no satisfactory basis upon which to classify pneumonias Whether we choose a clinical an anatomical or a bacteriological basis we shall invariably consider under each heading conditions that for some other reasons should be considered under one of the other headings In the face of this unsatisfactory state of affairs the division of the pneumonias into lobar and bronchopneumonia serves as well as any other division that could be proposed provided we use the terms to designate clinical as well as anatomical distinctions I wish only to emphasize that while clinically we hold to the concept of lobar pneumonia as a specific infectious disease circumstances compel us to consider also under this caption forms of lobar consolidation that do not properly belong here while we list under bronchopneumonia a heterogenous group of pulmonary inflammations with varying clinical course varying pathological picture and varying bacterial flora

Etiology

As has been explained bronchopneumonia is not a clinical entity and therefore the etiology as might be expected is not uniform Indeed the conditions causing this form of pulmonary inflammation are very diverse and complex Bronchopneumonia does occur in circumstances that give it the appearance of an independent disease but such occurrence is uncommon and for the most part it is secondary to some other disease or injury Following such disease or injury which somehow renders the lungs susceptible to infection bacteria of different kinds enter the lung and set up an inflammatory reaction When the bronchopneumonia is secondary to a specific infection the bacterium causing it is seldom the same organism that causes the specific infection Nor is it in many instances even a single variety of bacteria that invades the lung for commonly two or three sorts grow together in the same lung Bronchopneumonia is therefore in the anomalous position of being a quasi complication of many infectious diseases not due to the specific agent causing the primary infection and not due itself to any single organism The

occurrence the symptoms and the course of bronchopneumonia depend therefore in large measure upon the infection or trauma that precedes it and also in part upon the particular organism that happens to be the infecting agent

It might seem almost proper were we disposed to do so to lay all the emphasis in etiology upon the preceding infection or trauma and to slight as unimportant and accidental the particular organism that chances to be the infecting agent A willing advocate might say much in support of this view Certainly it is true that the clinical course of bronchopneumonia receives its characteristic marks as much from the infection with which it is associated as it does from the infecting organism For instance the bronchopneumonia complicating influenza runs a fairly typical clinical course but the clinician is unable to predict with much more than a random chance of being correct what the bacteriological study of the lung will reveal He cannot even invariably predict the anatomical features of the pneumonia whether it be lobar or lobular Furthermore an organism that will on one occasion produce a bronchopneumonia of the interstitial variety may on another occasion produce a bronchopneumonia of the lobular variety and on still another a frank lobar consolidation Perhaps most important of all in this connection is the observation that locality plays an important part in deciding the organism that is active in bronchopneumonia During the influenza epidemic of 1918 much confusion mingled with some criticism and recrimination was occasioned by the varying reports from different localities Blame for this discordance was put upon errors of technic, but this seems hardly reasonable particularly since some investigators obtained different results at different localities And in some localities the predominant type of organism apparently changed For instance MacCallum who studied pathological material at Camp Lee in Virginia Camp Dix in New Jersey and at the Johns Hopkins Hospital in Baltimore found the influenza bacillus predominantly at Camp Dix only occasionally at Camp Lee and not at all at Baltimore At the two last named places the pneumococcus and the streptococcus predominated

Having due appreciation for these well known facts and willingness to give them all the consideration they deserve I believe there is still room to place important emphasis upon the infecting organism Although a particular variety of pneumonia may be produced by a number of different organisms and a particular bacterium may cause different types of pneumonia still it is true that a particular variety of pneumonia

is usually due to a definite organism or at least to one of two organisms and that a given organism usually causes one variety of pneumonia For instance the pneumococcus is the important cause of lobar pneumonia often the cause of the lobular variety of bronchopneumonia and practically never the cause of the interstitial variety the hemolytic streptococcus is the important cause of the interstitial variety of bronchopneumonia yet very seldom the cause of lobar pneumonia the influenza bacillus causes the lobular variety of bronchopneumonia and often the interstitial variety also but it seldom causes lobar pneumonia Lobar pneumonia and bronchopneumonia often exist side by side in the same lung and the pneumococcus may be cultivated from the area of lobar consolidation the streptococcus or influenza bacillus from the area of bronchopneumonia The occurrence together of different organisms in bronchopneumonia may have an important influence upon the course of the disease as well as upon the pathological picture One variety of organism may inaugurate a pneumonia and then another variety may enter and supersede or modify the activity of the first invader When three or four organisms are present conditions become very complicated Opie[78] considers the role of the influenza bacillus in influenza pneumonia to be mainly of the nature of a preparatory influence He found the influenza bacillus almost regularly in the bronchial secretion but seldom in the pneumonic exudate where the pneumococcus and streptococcus flourished He looks upon the profound injury to the air passages—due he believes to the influenza bacillus—as the primary injury that allows other bacteria notably the pneumococcus the streptococcus and the staphylococcus to invade the lungs

In recent years important investigations have thrown fresh light upon the pathogenesis of the pneumonias that frequently complicate virus diseases especially measles vaccinia psittacosis pertussis and influenza It may be premature to include pertussis and influenza among the virus diseases but accumulating evidence indicates that they will soon definitely belong there The investigations to which I refer have demonstrated that a filter passing virus may produce extensive and characteristic changes in the lungs and that sometimes its influence is augmented and modified by a secondary bacterial invasion Shope[79] has shown that swine influenza which bears a striking resemblance to influenza in man can be readily transmitted by contact and also by the introduction of tracheal exudate from infected animals into the nasal passages of normal swine From diseased animals an organism can be regularly cultivated which is similar to if not really identical with the

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Finally certain general features such as age exposure and debilitating diseases are important contributory causes

Therefore the etiology of bronchopneumonia may be considered from many different standpoints and in order to present the matter satisfactorily each of these standpoints must be considered separately The accompanying table shows the factors in outline (Table II)

TABLE II

Etiology

I Aerogenous infections
  1 Primary bronchopneumonia
  2 Secondary bronchopneumonia
    A General predisposing causes
    B Infections
      1 Nonspecific respiratory infections
        Bronchitis
      2 Specific infections Bronchopneumonia due to
        a Specific organism
          tuberculosis
          plague
          diphtheria
          tularemia
        b Nonspecific organism
          typhoid
          dysentery
          diphtheria
          scarlet fever
        c *Virus infection*
          measles
          pertussis
          influenza
          psittacosis
    C Trauma
      1 Trauma to chest wall
      2 *Foreign particles aspirated*
      3 Fluids aspirated
      4 Gases

II Blood stream infections
  1 General sepsis
  2 Focal septic processes

III Bacteriology
  1 Pneumococcus
  2 Streptococcus
  3 Influenza bacillus
  4 Staphylococcus
  5 Other organisms

hemolytic influenza bacillus This organism will produce a disease in swine which may be mistaken for influenza but differs from it, since unlike the natural disease, it is not contagious The bacillus propagated on artificial media soon becomes nonpathogenic Suspensions of tracheal exudate and of lung from infected animals passed through Berkefeld filters, yield a filtrate that when introduced into the nasal passages of normal swine produces a disease resembling epidemic influenza though usually much milder This mild disease is contagious, and the influenza like bacillus cannot be grown from the tissues A combination of the filtrate and the bacillus produces in swine a disease in every respect identical with the natural epidemic influenza These experiments suggest that the actual cause of the disease is a filterable virus, but that the clinical manifestations do not fully develop until the influenza-like bacillus also comes into play Smith Andrewes and Laidlaw[230] have succeeded in transmitting a disease to ferrets by the intranasal instillation of throat washings from influenza patients The disease is transmissible from ferret to ferret either by contact or by the intranasal instillation of virus containing material The virus of swine influenza produces in ferrets a disease indistinguishable from that produced by the virus of human influenza McCordock and McKenfuss[1] have studied in detail the pathological characteristics of virus pneumonia in animals following the introduction of vaccine virus The lesions produced are identical with those that commonly occur at an early stage in influenza measles pertussis and other virus diseases The acute process he designates hemorrhagic virus pneumonia If this is followed by exudation and infiltration interstitial virus pneumonia develops This interstitial pneumonia is identical with the interstitial pneumonia described by MacCallum[22] and others as a frequent and characteristic complication of influenza measles and pertussis In pertussis typical inclusion bodies often are found in the pulmonary exudate The addition of bacterial infection to the virus pneumonia adds bronchitis bronchopneumonia abscess pleurisy empyema and bronchiectasis to the clinical picture

A third factor in the etiology of bronchopneumonia of sufficient importance to deserve notice, is the mode of infection I have so far spoken of bronchopneumonia as though it were always an infection by way of the respiratory passages In most instances the infection is conveyed by this channel but occasionally the infection arrives through the blood stream Septic bronchopneumonia as it is called occurs almost exclusively with general sepsis but occasionally it follows localized septic processes particularly after operation

tion is not restricted to the larger bronchi but descends to their finest ramifications Areas of bronchopneumonia are always associated with the bronchitis Probably in this condition particularly atelectasis plays an important role

2 *Specific infections* The specific infections are the most important precursors of bronchopneumonia in childhood and early adult life In infancy and childhood measles pertussis scarlet fever and diphtheria are the infections with which it is chiefly associated in adult life measles and influenza but it may occasionally be associated with any of the infectious diseases In only four of the specific infections namely plague tuberculosis diphtheria and tularemia is the bronchopneumonia due to the bacterium causing the primary disease and in all four of these infections nonspecific forms of bronchopneumonia also occur In diphtheria and tuberculosis the bronchopneumonia is often an aspiration pneumonia due in the one instance to the inhalation of particles of diphtheretic membrane in the other to aspiration of blood laden with tubercle bacilli following hemoptysis

C *Trauma* Under this heading I have put all injuries to the lungs whether the injury be inflicted by a blow upon the chest by the aspiration of foreign bodies or fluid or by the inhalation of irritating gases In many instances the aspirated material contains virulent organisms and the pulmonary injury and infection occur almost simultaneously in other instances the aspirated material is sterile or contains only avirulent organisms but the trauma makes the lung susceptible to invasion by virulent organisms entering through the bronchi

While injury to the chest is frequently followed by lobar pneumonia it is seldom followed directly by bronchopneumonia If the injury is severe associated conditions might easily lead to an aspiration bronchopneumonia

The aspiration of foreign material into the lung is a common cause of bronchopneumonia and occurs in the most varied circumstances It happens frequently in patients weakened and stuporous from a long illness in comatose patients after anesthesia following submersion and so on Aspiration pneumonia is a common sequel to operation around the nose and mouth and to abdominal operations when normal expulsive efforts to clear the bronchi are suppressed It follows the accidental inhalation of foreign bodies It occurs frequently in association with other pulmonary infections as the result of aspirating infected material as in bronchiectasis carcinoma and empyema rupturing into the lung

I Aerogenous infections 1 Primary bronchopneumonia In adults primary bronchopneumonia is almost unknown except in epidemic form, in children it occurs frequently during the first two years of life rarely after the fourth year In children the clinical symptoms are similar to those of lobar pneumonia, and the disease nearly always ends in recovery The pneumococcus is the usual infecting organism The epidemic form of bronchopneumonia in adults is a highly contagious disease caused by the streptococcus The disease begins usually as a secondary form of bronchopneumonia and then becomes established as an independent disease of great virulence In 1917 this form of pneumonia began in our cantonments as a complication of measles but quickly gained an independent footing spreading rapidly through the camps as a primary disease The recent investigations of virus pneumonia suggest that this form of bronchopneumonia is essentially a virus disease

2 Secondary bronchopneumonia A General predisposing causes Secondary bronchopneumonia is a common disease at all ages It occurs with special frequency at the two extremes of life In infants it is associated particularly with the specific infectious diseases, in old age particularly with bronchial catarrh and as a terminal event in chronic disease Debilitating influences of every kind and at every age predispose to bronchopneumonia

B Infections 1 Nonspecific respiratory infections Bronchitis The role that bronchitis or bronchial catarrh plays in the etiology of bronchopneumonia is sufficiently emphasized by the name In contrast to lobar pneumonia which hardly ever follows bronchitis bronchitis nearly always precedes bronchopneumonia In adults the bronchitis itself is usually secondary to some other condition either a part of some specific infection or a terminal event in some exhausting disease or the result of trauma In infants it may follow a primary bronchitis but the bronchitis is usually associated with some specific infection It is in old age that primary bronchitis plays its important role Even in old age however debility or some chronic disease is usually present which lowers the patient's resistance as we are accustomed to put it, and makes him an easy prey to bronchopneumonia when bronchitis develops As previously explained areas of atelectasis play an important part in the development of this type of pneumonia It is exceptional that a robust adult of any age develops bronchopneumonia after a primary bronchitis Perhaps one exception to this statement should be named the condition described clinically as capillary bronchitis This disease has a fairly characteristic clinical picture Unlike ordinary bronchitis the inflamma

is not so granular The bronchi leading to the areas of consolidation are inflamed and their lumen contains purulent material In some instances hypostatic congestion and atelectasis add further coloring to the varied picture In fulminating infections patients may die before real consolidation occurs The lungs are then deeply injected the alveoli filled with blood and hemorrhages and a hemorrhagic exudate are shown in the bronchial mucosa This condition has been named hemorrhagic pneumonitis

Two anatomical types of bronchopneumonia have been described interstitial pneumonia and lobular pneumonia

In *interstitial pneumonia* there is extreme infiltration of the bronchi leading to great thickening of their walls and distortion of the lumen atelectasis of the portion of the lung supplied by the obstructed bronchus the formation of small dense nodules about the terminal bronchioles hemorrhagic exudate into the surrounding alveoli and frequently a large pleural exudate at first seropurulent later more frankly purulent Rapid organization of the inflammatory exudate occurs the bronchial walls thicken the interlobular septa and the alveolar walls show a great increase in connective tissue and the lymphatics plugged with exudate become permanently occluded No large areas of consolidation occur

In *lobular pneumonia* the areas of consolidation are larger there is no formation of dense peribronchial nodules and the connective tissue reaction so characteristic of the interstitial variety is almost entirely absent These two types of bronchopneumonia are often found side by side in the same lung

Microscopically the exudate consists of leucocytes red blood corpuscles and desquamated epithelial cells The character of the predominating cell varies usually polymorphonuclear neutrophiles predominate but some exudates particularly in interstitial pneumonia are made up chiefly of small round cells The amount of fibrin is always less than in lobar pneumonia and is often entirely absent

Symptomatology and Physical Signs

The symptomatology of bronchopneumonia is as varied as its etiology Sometimes the symptoms are trivial and indefinite and the presence of bronchopneumonia may be only surmised at other times they are dramatic and fulminating It is impossible to convey a satisfactory impression of the symptoms and course of bronchopneumonia

Bronchial obstruction leading to retained secretion and atelectasis is usually followed by bronchopneumonia

II Blood stream infections occur in sepsis Infected emboli lodge in the lungs and produce areas of bronchopneumonia that frequently suppurate Less commonly, local septic processes associated with phlebitis may produce areas of bronchopneumonia These also usually suppurate

III Bacteriology The pneumococcus the streptococcus hemolyticus, the bacillus influenzae, and the staphylococcus aureus are the common causes of bronchopneumonia Occasionally almost every known pathogenic organism is found, namely, the meningococcus the plague bacillus the diphetheria bacillus Friedlander's bacillus, et cetera The organisms do not cause specific lesions or specific clinical symptoms although each organism has a favorite type of anatomical and clinical reaction The pneumococcus for instance causes lobar and lobular pneumonia, never interstitial pneumonia, the streptococcus causes chiefly interstitial pneumonia seldom lobular pneumonia the influenza bacillus causes lobular pneumonia more frequently than interstitial pneumonia but it often causes an interstitial pneumonia indistinguishable anatomically from streptococcus interstitial pneumonia Unless the disease occurs in epidemics the bacteriology cannot be predicted definitely from the anatomical lesion or from the clinical course Recent investigations suggest that interstitial pneumonia is a specific reaction to virus infection

Pathologcal Anatomy

The pleura may be smooth and glistening, but if patches of consolidation are near the surface of the lung they are covered with a thin fibrinous exudate In certain types of bronchopneumonia seropurulent exudates into the pleural cavity commonly occur The consolidated areas can usually be felt and on section they stand out more or less prominently as somewhat elevated patches differing in color from the surrounding lung tissue In color they vary from red to gray depending upon the proportion of blood and leucocytes in the exudate in size from pinhead areas to confluent patches involving a whole lobe When the areas are large, the cut surface has not the uniform appearance of lobar pneumonia, areas of consolidation in different stages varying with areas of air-containing lung Owing to less fibrin in the exudate the surface

lower lobes are nearly always the first to be involved and the tendency to this localization is an important point in diagnosis

Termination of the disease by crisis is unusual generally the symptoms disappear very gradually The areas of consolidation clear up slowly and often remain for a long time after the constitutional symptoms have disappeared

Primary bronchopneumonia in children has all of the clinical features of lobar pneumonia It is caused by the pneumococcus the symptoms are acute and severe and it ends nearly always in recovery

Aspiration bronchopneumonia has no characteristic symptoms If the patient is comatose or otherwise very ill only trivial symptoms may direct attention to the condition If the patient is robust and in good health all of the characteristic symptoms may develop If the *aspirated material is infected abscesses may form*

In terminal bronchopneumonia the symptoms are seldom striking A little fever the last few days of life or the development of cough are the common symptoms Usually there is a little dullness over one or both lower lobes suppressed breath sounds and moist *rales* sometimes outspoken signs of consolidation develop while at other times no abnormal physical signs can be discovered So commonly does bronchopneumonia occur as a terminal event in chronic renal and cardiac disease that clinicians often predict its presence even in the absence of definite symptoms or signs

Bronchopneumonia associated with the infectious diseases 1 Influenza In some severe cases pneumonia seems to begin with the onset of the illness More commonly it develops from the third to the fifth day sometimes later As a rule the symptoms come on insidiously In uncomplicated cases of influenza the temperature begins to fall on the third fourth or fifth day Persisting or increasing fever at this period at once awakens the suspicion that pneumonia is developing At the *same time the constitutional symptoms instead of improving grow* worse the patient becomes more deeply intoxicated cough and sputum increase the respirations become somewhat accelerated Bloody sputum which is frequently an early symptom always indicates pneumonia At this period the physical examination may disclose no definite signs or there may be only a few localized fine *rales* or suppressed breath sounds Later patches of consolidation become evident which may gradually spread and involve large areas of the lung At any stage the symptoms may subside either abruptly by crisis or more commonly by lysis The physical signs may persist for a long time

if it is to be treated as an independent disease Its protean clinical manifestations can be viewed fruitfully only in the setting under which they naturally occur There are, however, a few general marks that distinguish it from lobar pneumonia

The onset, in contrast to lobar pneumonia, is usually insidious In patients with chronic disease a little fever, a slight cough, accelerated respiration, bloodstained sputum, or the development of *rales* or a patch of bronchial breathing may call attention to the condition Frequently it is discovered at autopsy, when there were no particular symptoms to call attention to its presence during life In severe bronchitis it may be impossible to tell definitely that bronchopneumonia is present unless a patch of consolidation can be outlined We may safely assume that it is present with severe bronchitis of the small bronchioles even in the absence of definite physical signs In infectious diseases, as in influenza and measles, the first event to call our attention to the presence of bronchopneumonia may be continued fever and other evidences of intoxication at a time when uncomplicated cases of the disease begin to improve, or there may be bloody sputum, localized *rales*, a patch of consolidation tachypnea or cyanosis In interstitial pneumonia the severity of the constitutional symptoms and a pleural effusion may be the first evidence of bronchopneumonia

The fever is very irregular In terminal pneumonia is may be slight or absent It is sometimes continuous, sometimes remittent It is seldom as high as in lobar pneumonia, and the severity of the symptoms does not bear a constant relation to the height of the fever Occasionally patients die of bronchopneumonia when their temperature is normal

The pulse and respiration are usually accelerated but neither so con stantly or so strikingly as in lobar pneumonia Cyanosis is often extreme and out of all proportion to the dyspnea

The sputum is not characteristic Usually it is mucopurulent as in simple bronchitis Sometimes it is very tenacious When it is bloody, the color is bright red Characteristic rusty sputum is never seen Some times the sputum is hemorrhagic and profuse hemoptysis may occur

Percussion and auscultation yield inconstant and varying results At times no definitely abnormal pulmonary signs can be discovered even though the diagnosis may be made from the general symptoms At other times suppressed breath sounds persisting, localized *rales*, or areas of dullness and tubular breathing may be found The physical signs vary quickly from day to day, suggestive signs disappearing to reappear later or to be replaced by fresh signs in other locations The

disease are frequent often simulating tuberculosis They sometimes terminate in bronchiectasis Interstitial streptococcus bronchopneumonia is a common type just as it is with measles

4 Diphtheria In diphtheria bronchopneumonia may be due to an extension of the diphtheritic membrane to the bronchi This is a severe and almost consistently fatal form of the disease More commonly the bronchopneumonia follows the aspiration of infected material into the bronchi but the pulmonary inflammation is not caused by the diphtheria bacillus *Fever dyspnea and cough are the usual symptoms The physical* signs are the same as those described for influenza bronchopneumonia In diphtheria streptococcus bronchpneumonia is common

Epidemic streptococcus bronchopneumonia For centuries epidemics of pneumonia have been described that in the light of later experiences we may with reasonable assurance place in this class These epidemics have for the most part occurred when large numbers of recruits have been brought together and they have nearly always accompanied and followed epidemics of the exanthemata particularly measles A formidable epidemic started in Canada in 1812 and spread over the United States During the Civil War measles and pneumonia were common in the armies although the combined disease being overshadowed by the ravages of typhoid and dysentery did not attract particular notice In the winter of 1917 the cantonments throughout this country were visited by an extensive outbreak of measles followed by an epidemic of virulent streptococcus pneumonia This malignant and fatal form of pneumonia has occurred also in smaller and more localized epidemics among the civil population Finkler in 1888 reported several small outbreaks of the disease and described the severity of the clinical manifestations the pathological characteristics of the lung changes and the casual relation of the streptococcus The pathological characteristics of the severe bronchopneumonias following measles diphtheria and pertussis were first clearly described by Bartels[15] in 1861 He notes all the important characteristics of the lesions we now speak of as interstitial bronchopneumonia Finkler[16] and Durck emphasized the importance of the streptococcus as the cause of pneumonia As already stated recent observations suggest that this form of pneumonia is always primarily a virus disease

The epidemic in the United States Army Camps in 1917 followed immediately upon a widespread epidemic of measles All of the early instances came on as a complication of measles but once the pneumonia had become prevalent it began to attack healthy soldiers who had not

and are often discoverable by the roentgen ray months after the patient has recovered If the process spreads, the patient becomes more and more deeply intoxicated Cyanosis is often extreme The sputum becomes profuse and bloody Cough is harassing and uncontrollable The patient usually becomes delirious, but not infrequently he maintains clear consciousness almost to the moment of death In contrast to the cyanosis, the dyspnea, and the profound prostration, the heart action may remain astonishingly slow and vigorous The pulse may be slow and of excellent quality a few minutes before death Pulmonary edema is common and often extreme, frothy serum sometimes literally pouring from the mouth The leucopenia characteristic of influenza persists even after pneumonia has developed Empyema is rare, and abscess and gangrene occur far less frequently than in lobar pneumonia Subcutaneous emphysema is remarkably common Jaundice frequently comes on and is an ill omen Mortality is extremely high—from 25 to 40 per cent of those affected die

2 *Measles* Bronchopneumonia may develop at any stage of this disease, but comes on most frequently as the eruption begins to fade The persistence of high fever instead of its defervescence on the fifth or sixth day, particularly if the cough becomes aggravated, is very suggestive of bronchopneumonia Bronchopneumonia coming on at the height of the eruption is often accompanied by a rapid fading of the eruption an observation justifying the great danger the laity associate with the eruption striking inward The physical signs vary as they do in influenza bronchopneumonia The illness is usually accompanied by severe symptoms of intoxication Two special forms of bronchopneumonia occur with measles First following measles there is a tendency for tuberculous lesions to flare up and extend A disseminated tuberculous process in the lungs may simulate bronchopneumonia The duration of the symptoms will suggest the tuberculous nature of the lesion, but since bronchopneumonia may be prolonged into a subacute form the distinction is often difficult Second, epidemic streptococcus bronchopneumonia is often associated with epidemics of measles There are characteristic features to this type of pneumonia both clinically and pathologically

3 *Pertussis* Bronchopneumonia is a frequent complication of pertussis in infants less common after the second year and relatively uncommon after the fourth year It occurs usually during the period when the paroxysms are most severe The clinical course of the disease is similar to bronchopneumonia with measles Subacute forms of the

ventive inoculations but their value is far from demonstrated Since it has been shown that numerous strains of each type of organism exist and that each strain has distinct immunological properties it seems altogether unlikely that the injection of stock vaccines will produce any satisfactory immunity Similar vaccines have been used in treatment Their use is unscientific and of no appreciable value Serum of recovered patients has been used without demonstrable benefit The injection of nonspecific protein is also of doubtful value

In the absence of any remedial agent for bronchopneumonia the treatment must be confined to the general management of the situation The details need not be dwelt upon Absolute quiet both physical and mental must be enforced Plenty of fresh air and good nursing are important The diet must be planned to suit the patient semi solid foods may be given if the patient is in good condition Water should be freely given The bowels should be regulated with laxatives and enemata but purging is inadvisable Sponges may be given if the fever is high or for the nervous symptoms If the pain is severe the side may be strapped or better still a suitable jacket worn Digitalis may be given to prepare for the occasional onset of auricular fibrillation or flutter otherwise digitalis has not the least influence upon the disease Caffeine strychnine and camphor are popular stimulants so called but it is doubtful that they do the least bit of good and given in too large doses they may do harm The one drug that has definite value is opium It should be used freely but within the limits of discretion Codein heroin and morphine are the most useful preparations Unfortunately heroin is not available in the United States its exclusion being a part of the anti narcotic campaign

Abscess and Gangrene

It is difficult in the present state of our knowledge to draw a sharp distinction between pulmonary abscess and gangrene for the two conditions frequently occur together Acute diffuse gangrene that involves a lobe or a whole lung is a disease easily distinguished from abscess but if we attempt to separate circumscribed gangrene from abscess we are met by insuperable difficulties Nevertheless some diagnosticians insist it is essential that the distinction be made since important practical consequences depend upon it They claim that gangrene if recognized promptly and treated energetically by the use of arsphenamine may be

had measles The infection was most malignant It was characterized by symptoms of extreme intoxication, intense dyspnea, and cyanosis, with a remarkable tendency to pleural exudation In many instances the pulmonary lesions were completely obscured by a massive pleural effusion which began a few hours after the onset of the illness The effusion consisted at first of turbid serum containing innumerable streptococci which gradually became frankly purulent The pulmonary lesions, fully described by MacCallum were characteristic of interstitial bronchpneumonia and were often associated with areas of lobar or lobular consolidation The outstanding characteristic of the epidemic was the prevalence and extent of pleural effusions a condition entirely missed during the influenza epidemic the following year Almost regularly the Streptococcus hemolyticus was cultivated from the lung, although often the pneumococcus and other organisms were found associated with it

Staphylococcus bronchopneumonia Staphylococcus pneumonia is relatively uncommon but it has distinctive clinical features by which it may often be recognized and differentiated from other forms of pneumonia Usually it is secondary to some other condition that by its constitutional or local effects prepares the way for invasion of the lungs by the staphylococcus The features that characterize it are these (1) as in other forms of staphylococcus infection the fever is usually remittent (2) chills and sweats are common (3) abscesses frequently develop, (4) the staphylococcus predominates in smears and cultures from the sputum, and (5) the mortality rate is high although many patients recover

Treatment of Bronchopneumonia

The only sure prevention of bronchopneumonia is the prevention of the specific infections with which it is so frequently associated The control of diphtheria is an example of what may be done in this direction In drowsy and comatose patients care should be exercised in feeding Patients with acute respiratory infections should not be given anesthetics unless there is urgent need of operation During a recent epidemic of influenza much interest was arosed in the administration of vaccines The purpose was not to prevent the onset of influenza but to prevent the development of pneumonia Killed mixed cultures of the organisms chiefly implicated in the pneumonia—namely, the pneumococcus the streptococcus the influenza bacillus and the staphylococcus—were used Opinions vary widely about the benefit derived from such pre

fusiform bacilli recover after treatment with arsphenamine still this does not prove that the lesion was primarily caused by the activity of these organisms A lung abscess discharging good and laudable pus and containing only the ordinary pyogens is a very rare disease indeed Therefore while we distinguish upon good clinical ground between abscess and diffuse gangrene of the lung we shall not attempt in this discussion to separate abscess from circumscribed gangrene

Pathological Anatomy

The gross appearance of pulmonary abscesses depends upon their etiology and the stage of development Acute abscesses appear as gray yellowish or red areas of softening from which pus can be expressed When cavities form they may be single or multiple or communicating They vary greatly in size At an early stage the walls are ragged and soft and not sharply marked off from the surrounding tissue Old abscess cavities may be smooth and surrounded by an area of dense fibrosis Bands containing branches of the pulmonary artery and thrombosed veins often run through the cavity The lung tissue around the abscess is infiltrated and fibrosed There is always marked induration of a lobe or of the whole lung Abscesses frequently lie beneath the pleura and the pleura is often involved The pleurisy may be dry or there may be a purulent or gangrenous pleural exudate

Laennec divided gangrene into two classes diffuse and circumscribed and this division is still adhered to In the diffuse variety a whole lobe or a still greater area of the lung may be involved with no sharp demarcation from the surrounding unaffected area The gangrenous area presents a greenish gray or brown color and is soft and pulpous In the circumscribed variety one or more areas of varying size exist that are at first dry and greenish gray in color later moist soft greenish brown or black in color with central softening and cavity formation These areas are limited by a zone of pulmonary infiltration and edema and in chronic cases by a pyogenic membrane

Pulmonary abscesses may be found in any of the lobes although the middle lobe is seldom involved Aspiration abscesses particularly postoperative are more frequent in the upper lobes than in the lower about two to one postpneumonic abcesses occur more frequently in the lower lobes than in the upper about two to one They are more commonly situated near the pleura than deep in the lung substance

cured in a large proportion of the cases, whereas the treatment for abscess is quite different The differentiation is based upon the character of the infecting organisms Abscess, they say, is caused by pyogenic organisms usually the staphylococcus gangrene by spirochetes fusiform bacilli, vibrios and anaerobic bacteria The diagnosis may usually be made from the character of the sputum In abscess it is yellowish purulent or mucopurulent, with little or no oder, in gangrene it is thin, gray-brown or gray green and foul smelling

The chief difficulty in making such a sharp distinction is our lack of precise knowledge about the way lung abscesses come about and the organisms originally responsible for them Nothing could be more confusing than the results of the most careful bacteriological investigations Perhaps some order might be brought into this confusion if the infection could be studied at its earliest stage To do this, however is almost impossible and when the abscess has once communicated with a bronchus the possibility of secondary infection can no longer be excluded More than this such a plan of study would be valuable only if the abscess were embolic for infection by way of the air passages brings in at once a host of bacteria and it is impossible to decide which among them are responsible If we use the presence or absence of spirochetes and fusiform bacilli as the deciding criterion to distinguish between abscess and gangrene we are upon insecure clinical ground The fact that these organisms may be absent at first and present later suggests that they are secondary and often only temporary invaders When present they often may be driven out by arsphenamine, and yet there may be no change whatsoever in the condition of the patient at least none that we can detect by any clinical methods of examination It is possible indeed even probable that the settling of spirochetes and fusiform bacilli in an abscess adds something of importance to the situation You may if you will speak of this as gangrene added to abscess and, if the infection is eliminated say the gangrene is cured but the abscess remains This way of looking at the matter however even though the facts be true would not establish abscess and gangrene as two independent diseases for a condition might be abscess at one moment and gangrene at another There seems little reason to doubt that diffuse gangrene is the result of the combined and unrestricted action of spirochetes fusiform bacilli and other organisms but to draw a sharp distinction between abscess and gangrene merely upon the evidence of the presence or absence of these organisms seems to me to lead only to clinical confusion Even though patients with foul sputum swarming with spirochetes and

In a series of 76 male and 35 female patients comprising all of the cases of pulmonary abscess entering the University of California Hospital from 1 January 19 7 to 1 January 1948 48 cases were ideopathic 36 followed some surgical procedure and 6 followed aspiration of a foreign body

We may assume that infected material entering the lungs penetrates deeply into the bronchial tree and finally lodges in one of the smaller branches We have already referred to the important part that bronchial obstruction plays in facilitating pulmonary infection and although direct proof is lacking still the results of experiments and also the fact that abscess often develops in collapsed portions of the lungs justify the assumption that bronchial occlusion and atelectasis comprise the first stage in the development of an abscess What follows will depend in large measure upon the organisms present in the infected material In children pure pyogenic abscesses are said to occur frequently but in adults spirochetes fusiform bacilli and various anaerobes are nearly always present The bronchi and collapsed alveoli become filled with leucocytes and fibrin the inflammatory exudate undergoes liquefaction and a small cavity is formed which gradually extends As the inflammation progresses scar tissue forms which may compress other bronchi and thus numerous small abscesses may form and coalesce producing a large irregular ragged cavity surrounded by dense fibrous tissue

The development of an abscess in an area of pneumonic consolidation cannot be so clearly followed It usually comes on gradually and perhaps the first stage is organization of the exudate and the production of bronchial obstruction It has been suggested that thrombotic occlusion of an artery supplying a part of the consolidated lung may be the underlying cause of abscess in pneumonia the disturbed circulation allowing secondary invaders to gain an easy foothold

Abscess of the lung usually follows operation or pulmonary inflammation In a consecutive series of 17 cases of lung abscess Flick Clerf Funk and Farrell[1] found that 121 followed surgical operation 43 followed acute respiratory infections and 8 followed miscellaneous conditions namely chest injury drowning poisoning with sewer gas and unknown causes Of those following operation 97 followed tonsillectomy 10 followed operations upon the mouth and 14 followed operations elsewhere Of those following respiratory infections 2 followed cold influenza or bronchitis 16 pneumonia bronchopneumonia and 1 acute pleurisy

Pathogenesis

Lung abscess may be produced easily by introducing infected material into the veins. The method commonly employed is to insert clots of blood inoculated with bacteria or bits of agar similarly prepared. Infected emboli always cause changes in the lungs: (1) local consolidation may occur from which the animals quickly recover, (2) a hemorrhagic infarct may form which (a) may heal or (b) go on to abscess formation, and (3) a massive hemorrhagic consolidation may occur which is rapidly fatal. The formation of a chronic abscess seldom follows the introduction of emboli saturated with a pure culture of any of the usual organisms, namely, staphylococcus, streptococcus, colon bacillus, et cetera. A mixture of different organisms is more often successful. Abscess follows regularly when mouth organisms, including spirochetes, are used. Sterile emboli cause only slight local circulatory changes in the lung. Abscess may form in the area, however, if organisms, especially scrapings from the teeth, are injected later into the blood stream or introduced into the bronchi.

The production of lung abscess by the bronchial route is difficult. The introduction of pyogenic bacteria is never successful, even when the bronchus is ligated or plugged with a foreign body. The introduction of organisms with lipiodol is said to be followed regularly by suppuration and sometimes by the formation of an abscess cavity. Since up to the present time similar results have been obtained only by using mouth organisms containing spirochetes and fusiform bacilli, it is possible that these organisms may have been introduced unintentionally with the lipiodol. The objection to experiments in which mouth organisms are used is that the lesions produced are gangrene and not abscess.

It is probable that pulmonary abscess in man may be caused both by embolism and by aspiration. Perhaps in some instances both factors may work together, the area of the lung supplied by an artery that is plugged with a sterile embolus becoming infected by aspirated material. There is not yet a settled opinion about the relative frequency with which abscess is caused by embolism and by aspiration, although most observers believe that the bronchial route is the usual way. There is much indirect evidence to favor this view, especially the fact that abscess so often follows operation upon the upper respiratory tract. Kline[19] has summarized the arguments and thinks they justify the conclusion that in nearly all instances infection occurs by aspiration.

have seen in which it came on after a *long automobile drive* and was due *probably to the aspiration of some small foreign body of which the* patient was unconscious A few days or some weeks after operation (on an average seven days later) the patient has pain in the chest or begins to cough and has fever The fever persists the cough becomes more and more severe and varying amounts of mucopurulent sputum are raised The leucocytes are moderately increased in number the polymorphonuclears predominating Physical signs may reveal no pulmonary abnormality or there may be evidence of local infiltration and consolidation The diagnosis of bronchopneumonia is usually made At the end of a week the temperature becomes irregular the cough is more severe and larger amounts of sputum are expectorated About the fourteenth day the sputum usually acquires a characteristic fetid odor and the diagnosis of abscess can then be readily made During the third or fourth week the symptoms as a rule begin to change somewhat The temperature becomes frankly septic in type and displays variations in proportion to other symptoms Cough may become less annoying and large amounts of sputum may be brought up at one time Usually the sputum has a disagreeable odor Often these symptoms go along in a *recurring sequence* The patient will expectorate a large amount of fetid *sputum the temperature will drop cough will diminish* and the patient will experience sensations of relief and relative well being The temperature may remain at a nearly normal level for a day or two and give rise to the hope that recovery is on the way Then gradually the temperature mounts again the symptoms of intoxication return cough becomes harassing but only a little mucopurulent sputum comes up until after a number of days suddenly a large amount of fetid sputum is expectorated and temporary improvement again begins During this *period the sputum is often bloody and occasionally frank hemoptysis* occurs although large hemorrhages are nearly always restricted to later stages of the disease

During the second month of symptoms many abscesses gradually heal The symptoms slowly recede and finally the temperature remains normal Cough and sputum disappear and the general health is rapidly restored Sometimes an abscess will rupture into the pleura and will heal when drainage of the pleural cavity is established Sometimes an abscess *produces widespread pulmonary suppuration and gangrene and may be* rapidly fatal

Abscesses that do not heal within two or three months enter a chronic stage and hope of spontaneous cure must then be abandoned

Less frequent causes of abscess and gangrene are bronchiectasis (which is commonly followed by gangrene) septic emboli, the rupture of contiguous areas of suppuration into the lung, and a host of chronic pulmonary diseases in which secondary infection occurs In the last named group may be mentioned cancer, sarcoma, dermoid cysts tuberculosis, syphilis echinococcus cysts fungus infection et cetera Empyemata frequently rupture into the lung as do abscesses in the liver and subphrenic abscesses Perforation of the esophagus vertebral caries and suppurating bronchial glands may also give rise to abscess and gangrene Pulmonary infarcts occasionally become infected and produce abscesses Infection anywhere in the body may cause embolic pulmonary abscesses from infected venous thrombi They are usually multiple and play a secondary part in the clinical features of the primary infection

Bacteriology

Identification of the bacteria present in lung abscess has been carried out by careful examination of washed sputum of secretion secured at operation and of material aspirated through the bronchoscope For instance Varney [5] and Cohen [39] have made careful studies and Marshall and Brunn [57] have critically reviewed the results so far obtained No single organism is ever present alone The bacterial flora consists of *many different organisms aerobic and anaerobic the anaerobic* usually predominating In untreated cases aerobic and anaerobic streptococci fusiform bacilli bacillus melaninogenicum and spirochetes predominate in treated cases spirochetes fusiform bacilli and bacillus melaninogenicum decrease in number or disappear entirely while the streptococcus hemolyticus is relatively increased In a word the bacterial flora of lung abscess especially when untreated closely resembles that of infected tonsils cervical abscess and diseased teeth

Symptoms

The symptoms and the clinical course of lung abscess depend somewhat upon the cause They are more distinctive and more characteristic in aspiration abscess than in other forms because that condition has the character of an independent and primary disease Occasionally an abscess will develop without known provocation as in one instance I

phasized again that abscesses frequently occur in the upper lobe

The characteristic features of the sputum are the odor and the occurrence of shreds of pulmonary tissue Its appearance is by no means uniform It may be thin and purulent or tenacious and varies in color from pale green to brown and almost black depending largely upon the amount of blood and the changes the blood pigment has undergone As it stands it usually separates into three layers on top masses of discolored frothy sputum dipping down in strands into the middle layer of cloudy watery fluid and a heavy sediment of pus at the bottom Shreds of pulmonary tissue may be large enough to be recognized by the unaided eye When the sputum is allowed to stand these and smaller masses fall to the bottom and they may be identified by the demonstration of elastic fibers Dittrich s plugs may also be found These are soft put y like masses made up of bacteria fatty acids free fat, and debris of a most disagreeable odor

Roentgenological examinations are of the greatest help in the diagnosis of pulmonary abscess and are indispensable in the treatment of the condition An abscess casts no characteristic shadow by which it may be recognized but its location and the condition of the surrounding lung tissue will often help to distinguish it from empyema and tuberculosis Not infrequently abscess is diagnosed clinically and the roentgen ray will demonstrate the presence of an unsuspected foreign body in a bronchus This occurs over and over again in young children If operative treatment is indicated, the roentgen ray will tell better than any other method of examination the location of the abscess whether it is single or multiple and the best route of approach

Pulmonary hemorrhage and brain abscess are the two most common complications of lung abscess Fatal hemorrhage usually occurs only in chronic abscess when it is due to the rupture of an aneurysm of a branch of the pulmonary artery traversing a cavity In gangrene fatal hemorrhage may occur at an earlier stage Although general sepsis is uncommon brain abscesses are often multiple Clubbing of the fingers often occurs early and rapidly in lung abscess

Treatment

The aim of treatment in pulmonary abscess is (1) to maintain and if possible to improve the general strength and nutrition of the patient

When pulmonary induration becomes well marked complete obliteration of the abscess cavity is not likely to occur The patients from then on have symptoms like those in bronchiectatic dilatation They have cough with profuse expectoration, which is sometimes restricted to certain times of the day For instance they may empty the cavity or cavities two or three times a day and be free from cough during the intervals Unfortunately, even such a relatively satisfactory state of affairs seldom exists The sputum is often transiently or permanently so foul that the patients are social outcasts, they have recurring attacks of fever that undermine the general health, hemorrhages are frequent, they are constantly in danger of the more serious symptoms of rapidly spreading pulmonary infection As a rule, they live a few ungrateful and unwelcome years and exhausted by their disease, finally die of bronchopneumonia

The symptoms of abscess following lobar pneumonia are not nearly so distinctive At the termination of the acute symptoms of the disease fever persists and the consolidation fails to resolve Empyema induration abscess and tuberculosis are suspected The fever is usually irregular there is increasing cough and mucopurulent sputum and the leukocyte count remains elevated The diagnosis is definitely made when the sputum acquires the characteristic odor or when large amounts of purulent sputum are expectorated at one time The evacuation of the abscess may be followed by recovery or the abscess may go on to the chronic stage already described

As has been pointed out localized gangrene nearly always goes hand in hand with abscess formation It gives the characteristic odor to the sputum When gangrene oversteps these local bounds and becomes widespread, more serious symptoms supervene The temperature is higher, the evidence of more severe intoxication is apparent the patients lose flesh and strength more rapidly and the disease is more often quickly fatal The sputum is usually more fluid than in abscess of a greenish dirty brown or prune juice color The fetid odor is intense and may penetrate a whole house

Physical Signs

The physical signs of abscess are not at all distinctive In the early stages no, or only slight abnormalities may be discovered Later the signs are those of local consolidation or of cavity It may well be em

especially if the abscess is in an upper lobe Lower lobe lesions drain most satisfactorily with the patient in the prone position his head lowered Mid lung abscesses may drain best if the patient lies on the healthy side although patients usually learn by experience to assume this position spontaneously

Recent advances in chemotherapy have been of the utmost value in the medical treatment of pulmonary abscess Penicillin should be given in large doses from the onset especially if it can be shown that the majority of the organisms involved are not penicillin resistant If possible it is advisable to determine this factor The dosage schedule is the same as that employed in severe pneumonia and the treatment should be continued until the abscess is proved by x ray to be healed From 500 000 to 1 000 000 units of penicillin a day are probably advisable If the majority of the organisms are resistant to penicillin but susceptible to streptomycin the latter may be used either alone or as dihydrostreptomycin in doses of . gm per day given at 1. hour intervals for several days, followed by 5 gm doses at 1.-hour intervals for as long as necessary It should be remembered however that in large doses and sometimes in moderate doses streptomycin affects the vestibular apparatus and that dihydrostreptomycin when given over long periods of time in doses greater than 1 gm a day may cause deafness

Surgical Treatment Medical treatment may be followed as long as the abscess is acute that is as long as it is not more than six weeks old and shows signs of healing as revealed in serial roentgenograms Whereas it was formerly estimated that 20 to 5 per cent of pulmonary abscesses healed spontaneously it is now probable that at least ,0 per cent will heal without surgery Nevertheless if healing does not continue or if the abscess becomes larger surgery is indicated Certainly healing by medical means is unusual after an abscess is three or four months old It should be borne in mind too that the technical procedure is less formidable in a recent abscess than in an older one If possible it is advisable to have surgical consultation from the beginning

No arbitrary time period period from the onset can be set for surgical intervention each case must be treated individually Neuhof ' considered an abscess acute if it was less than six weeks old while Sweet extended the period to four months Others however have been inclined to disregard the time element—a point of view that seems rational While in the past physicians held incision and drainage as to be the acceptable method of surgical treatment, first making sure that the pleura was adherent at the point of incision more recently they have

(2) to secure adequate drainage, (3) to combat the underlying infection, and (4) to remove the suppurating area if more conservative methods fail

As soon as the diagnosis of pulmonary abscess is made bronchoscopy should be done at once to rule out the presence of a foreign body and the presence of malignancy since the first manifestation of bronchogenic carcinoma is often the development of a pulmonary abscess If a foreign body is present and is removed, the distal abscess will usually clear promptly but should receive adequate treatment in order to prevent its becoming chronic The modern treatment of pulmonary abscess will often lead to cure even in the presence of malignancy, the so called false cure of primary bronchogenic carcinoma which is unfortunate It is therefore essential to rule out bronchogenic carcinoma at the outset

Medical Treatment At an early stage and indeed throughout the duration of the illness care of the general health is essential Fortunately many abscesses heal spontaneously There can be little doubt that measures that improve nutrition keep the blood in normal condition, and facilitate the proper play of bodily functions aid the process of healing If at a later stage of the disease exacting methods of treatment must be used, they will be better tolerated if strength and nutrition have been maintained Measures to be employed are those that are now generally used in the treatment of tuberculosis or acute pneumonia Bed rest and as liberal a diet as the patient can be induced to take are of course essential It is not necessary to go into details for the principles are well understood, but it requires ingenuity and patience to carry out successfully the details of nursing and diet Small blood tranfusions are helpful Morphine should be withheld although troublesome cough may be combated by sedatives and codeine It is important however, to realize that a certain amount of coughing is essential Inhalants vaccines and arsenicals the last named to act on anaerobic bacteria, have been used in the past but it is doubtful if they are of much value

Postural drainage is a valuable adjunct in medical therapy On the other hand, the exhausting procedures sometimes employed in the past in the belief that drainage could be better promoted are not considered to be worth while As a rule the intelligent patient will quickly learn what position best facilitates drainage with the least effort on his part This may not always be the anatomical position that the physician thinks best Occasional changes of position from side to side or a change to the prone position may be all that is necessary Withdrawal of the pillow from time to time may aid A semi-recumbent position may be best

and extensive pleurisy Syphilis and pneumonoconiosis are less common but important causes Smaller areas may follow the most diverse pulmonary lesions Small areas of induration give no important symptoms larger areas lead to retraction of the chest wall diminished mobility dislocation of the mediastinum dullness and diminished or blowing breath sounds Bronchiectasis commonly occurs in association with cirrhosis and explains the cough and sputum that are frequently present The other important effect of induration especially when it is diffuse is the production of emphysema and by interference with the pulmonary circulation, hypertrophy and dilatation of the right side of the heart When the condition is extensive dyspnea and cyanosis are present

Secondary chronic inflammatory disease of the lungs, or, as it is often called *chronic pneumonia*, is usually a step on the way to cirrhosis Unresolved lobar pneumonia is the most common cause There is no sharp distinction between chronic pneumonia and induration Some authors restrict the term chronic pneumonia to instances in which symptoms particularly fever persist Bronchopneumonia may be followed by a similar train of events It is important to emphasize that the term chronic pneumonia covers a host of diagnostic errors Frequently the original disease which has failed to resolve was not a genuine pneumonia Tuberculosis is often the cause of the condition

Primary chronic inflammatory disease of the lungs is an unusual but in many respects an important condition Owing to the similarity of its symptoms with those of pulmonary tuberculosis the condition has been described frequently as chronic nontuberculous pulmonary disease The onset may be gradual or abrupt In most instances it comes on gradually with symptoms that cannot be distinguished from those of an ordinary cold less frequently it begins with symptoms suggesting a mild bronchopneumonia Instead of the symptoms subsiding promptly as they do in an ordinary acute respiratory infection they persist indefinitely Patients have been under observation for ten years with little change in their symptoms There is usually fever and cough and expectoration which vary in intensity from time to time Blood spitting is common and sometimes there is profuse hemoptysis In spite of the prolonged fever the patients are usually in good general condition and complain only of the cough and sputum Examination nearly always reveals lower lobe lesions slight dullness harsh or diminished breath sounds and numerous moist *rales* The symptoms vary in intensity from time to time sometimes disappearing almost completely Attacks of pleurisy are common One patient after having been under observation for six years died of a

come to prefer lobectomy In the chronic stages of the disease, that is, in abscesses more than two to four months old, there is a good deal of intrapulmonary fibrosis, bronchiectasis, and secondary alterations in the pleura In such cases inadequate drainage produces periodic exacerbations of the disease each one leaving the patient in worse condition than before Recurring hemoptysis is common together with bouts of low grade fever anorexia and debility Dyspnea and cyanosis may occur with cardiac insufficiency, amyloid degeneration is not uncommon and brain abscess may be a terminal event In this stage drugs have little effect Although penicillin may produce amelioration of symptoms the only definitive treatment is surgery preferably lobectomy

Results of Treatment The increasingly favorable results of treatment of lung abscess by means of antibiotics and moderate surgical techniques have not yet been fully recorded in the literature Neuhof and Touroff [9] reported 86 consecutive operative cases of acute putrid pulmonary abscess in 1941 73 or 85 per cent, were cured and 10 were improved There were only 3 postoperative deaths More recently the same authors reported 104 operations with only 4 deaths Certainly the exact localization of the abscess the vigorous use of chemotherapy, and the employment of pulmonary resection without undue delay should markedly change for the better the outlook in pulmonary abscess

Chronic Inflammatory Conditions in the Lungs

Under this heading is collected a heterogeneous group of diseases or rather conditions, varying in etiology, in pathological anatomy, and in clinical symptoms A portion of the cases represents a later stage of some acute process and they are best treated under the heading of the diseases they follow Another portion represents no inflammatory condition but the scarring and induration that follow inflammation Still another portion however although a small portion represents an apparently independent disease the process starts as a low-grade infection and persists for years without definite healing In classifying chronic inflammatory pulmonary disease we shall divide them into (1) pulmonary cirrhosis induration or fibrosis (2) secondary chronic inflammatory diseases and (3) primary chronic inflammatory diseases

Pulmonary cirrhosis or induration follows the healing of any chronic pulmonary inflammation The common causes of induration of large areas of the lungs are unresolved pneumonia pulmonary tuberculosis

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rapidly fatal empyema At autopsy the bronchi in both lower lobes were dilated and filled with purulent material Around the dilated bronchi were scattered areas of bronchopneumonia Sputum cultures show pneumococcus influenza bacillus and streptococcus, often in pure culture There is no satisfactory treatment for the condition The symptoms may be allayed by proper remedies General measures directed to building up the patient s condition are the most important Vaccines have disappointed me

SPECIFIC INFECTIONS

Syphilis

Syphilis of the lungs is occasionally diagnosed clinically, it is seldom recognized with certainty at autopsy An indurative pulmonary lesion particularly when it is situated in the lower or middle lobes occurring in an individual who has a syphilitic infection that clears up promptly upon the vigorous administration of anti syphilitic remedies is assumed to be syphilis of the lung Anatomically however syphilitic lesions are difficult to distinguish from tuberculosis and from other forms of pulmonary induration and no doubt much of what was formerly described as syphilitic phthisis was in reality tuberculosis In contrast to tuberculosis which is common in the lungs but rare in the upper respiratory passages syphilis is common in the upper passages and rare in the lungs It not infrequently causes ulceration in the trachea and the point of bifurcation is a favorite location As the lesion heals contraction occurs and one of the main bronchi may become occluded As a result there develops extensive bronchiectasis and fibrosis of the lung

Pathology

The most characteristic lesions of syphilis of the lungs occurs in the congenital form These lesions consist of gummatous nodules, extensive induration and the desquamative process spoken of as white pneumonia ' They often occur side by side in the same lung Definite localized gummata are rarely found The condition usually consists of induration and desquamation of alveolar cells The lungs are large and firm and white Microscopically the alveolar epithelium is cubical in form and the alveoli are filled with desquamated epithelial cells and a few leucocytes and mononucelar cells The alveolar septa are tremendously

thickened and there is marked proliferation of the connective tissue around the bronchi and blood vessels The blood vessel walls are greatly thickened and many are occluded Babies with such extensive lesions are born dead or die shortly after birth but when the lesions are less marked they may live It has been suggested that syphilis may be the underlying cause of extensive pulmonary induration and bronchiectasis which occasionally develop insidiously in young children Late forms of hereditary pulmonary syphilis that come on at puberty or later are described These instances have the characters of the acquired form

Acquired syphilis of the lungs may occur as gummata as diffuse or local induration and perhaps as a gelatinous pneumonia The occurrence of syphilitic gelatinous pneumonia is much discussed but it has neither clinical nor anatomical features by which it may definitely be recognized Gummatous lesions seldom occur apart from indurative lesions They vary in size from tiny nodules to tumors as large as an egg These nodules are usually situated near the hilus and in the lower lobes and are always associated with marked fibrous tissue proliferation In the course of time they degenerate and caseate and are finally replaced by dense scar tissue In this way large bands of connective tissue may run throughout the lung and by compressing the bronchi lead gradually to a diffuse bronchiectasis The walls of the blood vessels participate to a striking degree in the connective tissue proliferation and many of the vessels become obliterated When this process is extensive and diffuse the pulmonary circulation may be seriously interfered with and the right side of the heart may gradually become enlarged This extensive pulmonary fibrosis cannot be recognized definitely as syphilitic The diagnosis depends upon the absence of the evidence of tuberculosis upon the occurrence of syphilitic lesions elsewhere and occasionally upon the demonstration of the spirochete

Symptoms

When the hereditary form is well developed the babies are born dead or die shortly after birth So called late hereditary forms of pulmonary syphilis do not differ from the acquired form

During the secondary manifestations of the syphilitic infection bronchial catarrh cough and expectoration are frequently present These symptoms are occasioned by the presence of the syphilitic efflorescence

upon the bronchial mucous membrane The symptoms disappear as the eruption clears up

In the late syphilitic pulmonary affections there are no characteristic symptoms The disease is assumed to be present when tuberculosis is excluded and when the patient has the signs of a syphilitic infection elsewhere or a positive Wassermann test The correctness of the diagnosis is then tested by the effects of treatment

There are, however certain features of the pulmonary lesion that may suggest its syphilitic nature The lesion is much more commonly situated in the middle and lower parts of the lungs leaving the apices free This is in striking contrast to chronic tuberculous processes, which almost uniformly involve the apices The lesions are characterized also by marked dullness with diminution in the intensity of the breath sounds and the paucity of *rales* The presence of fever over a long period of time with little deterioration of the general health is another suggestive symptom Whenever a patient has a chronic indurative pulmonary lesion with tubercle bacilli constantly absent from the sputum, syphilis should be suspected A careful investigation for other evidence of syphilitic infection the Wasserman test and the results of treatment will decide the diagnosis The frequent association of tuberculosis and syphilis in the same patient should be emphasized

Syphilis of the lungs usually occurs in two forms, a subacute form simulating ulcerative phthisis and a chronic form coming on insidiously as a pulmonary fibrosis The clinical symptoms of the former type are those of pulmonary tuberculosis There is cough dyspnea cyanosis fever and loss of weight and strength As has been noted, the location and character of the lesion may suggest at once a nontuberculous infiltration Fever is usually less marked in syphilis than in tuberculosis and the wasting is less striking On the other hand dyspnea is more prominent Hemoptysis occurs but apparently not so frequently as in tuberculosis When fever is present it yields almost at once to iodides and in some cases this may serve as a therapeutic test

In the chronic indurative form of the disease the symptoms resemble those of fibroid phthisis The patients have cough and expectoration and as bronchiectasis usually develops they may have the symptoms and signs of cavity The sputum is sometimes putrid There may be an irregular, septic temperature and the patients may become markedly emaciated In these chronic cases the pleura is often involved, and great thickening of the pleura may accentuate the pulmonary sclerosis

The sclerosis of syphilitic disease always involves the branches of

the pulmonary artery to a marked degree In rare instances the pulmonary involvement is relatively insignificant and the disease consists primarily of a diffuse and generalized sclerosis of the pulmonary arterioles This condition gives no physical signs and usually passes unrecognized until cardiac symptoms develop Even then the true state of affairs is usually overlooked and the myocardial insufficiency is ascribed to disease of the heart muscles At autopsy the tremendous hypertrophy and dilatation of the right heart and the extensive disease of the pulmonary arteries explain the sequence of events

Warthin[305] has described a remarkable case diagnosed as mediastinal tumor and later as Osler Vaquez disease The clinical course was characterized by attacks of angina hypercyanotica cyanosis increasing weakness drowsiness edema asthma dyspnea enlargement of spleen and liver multiple telangiectasias and constant erythremia The autopsy revealed extreme atherosclerosis of the pulmonary artery and all its branches extreme dilatation of the right heart fibrosis and emphysema of the lungs extreme angiectasia of the entire vascular system enlargement of the liver and spleen and hyperplasia of the bone marrow Microscopically the changes in the pulmonary arteries were typically syphilitic Warthin regards the syphilitic pulmonary arteritis as the first link in the chain of symptoms and points out that the symptoms correspond with those described in Spanish American literature as Ayerza s disease or cardiacos negros

Treatment

There is nothing peculiar about the treatment of pulmonary syphilis It is the same as the treatment of the disease elsewhere The only point that needs emphasis is the importance of making the diagnosis before the process becomes very advanced

PNEUMONOMYCOSIS

Fungi sometimes invade the lungs In this country such infections are reported only rarely but they are frequent enough to deserve consideration especially since they are difficult to recognize and are therefore often overlooked Satisfactory classification of the fungi is at the present time impossible Many orders and varieties have been described and the conflicting names that have been proposed lead to inextricable

confusion The types that have most often been found in the lungs are (1) The molds (chiefly varieties of aspergillus penicillium and mucor To this group we may add also sporothrix, although it does not strictly belong here) ( ) The yeasts (chiefly *Blastomyces coccidioides* and torula) (3) The streptothrices (chiefly streptothrix or lepothrix and actinomyces) For further discussion see chap xiv in vol v

The diagnosis of fungus infection of the lungs is difficult There are no characteristic symptoms by which it may be recognized Of the clinical features of the condition it may be said that a fungus infection should always be suspected when there is pulmonary disease that does not readily and easily fit into one of the accepted diagnostic categories and that suspicion should stimulate the effort to demonstrate the pres ence of fungi in the secretions Although it is essential to the diagnosis that the presence of the micro organism be established, still even when present it may sometimes escape detection and at other times even when found it may not be the cause of the pulmonary lesion The rela tion of fungi present in pulmonary secretion to the underlying pulmo nary disease is threefold (1) The fungus may be present in the secre tion as a saprophyte and have nothing to do with the lung lesion (2) The fungus may have entered the lung as a secondary invader but having gained a foothold it may mingle with the previously existing disease and cause important and profound alterations in the course of events (3) The fungus may be the primary and the sole infecting agent in the disease

Fungi frequently inhabit the respiratory passages as saprophytes but their occurrence in sputa is not conclusive evidence that they are the cause of the disease under consideration Whether in these circum stances their presence is altogether innocuous cannot be definitely de cided It has been suggested that they may be harmful through the elimination of toxins or ferments thus causing local irritation and per haps even remote deleterious effects Steinfield in studying cases of chronic bronchitis with asthma, frequently found in the sputum various yeasts particularly monilia cryptococcus and endomyces The symp toms were greatly relieved by the administration of iodides Fungi fre quently enter the lungs as secondary invaders complicating the pre existing disease They are commonly associated with tuberculosis but occur also with bronchitis bronchiectasis abscess carcinoma, et cetera Fungi are less frequently the primary and independent cause of pulmo nary disease The lesions they produce are varied and the clinical symp toms may resemble bronchitis bronchiectasis, tuberculosis, broncho

pneumonia abscess pleurisy empyema and new growth The disease is usually chronic and, as fibrosis is extensive the terminal stage may be the clinical picture of pulmonary cirrhosis

The disease in most instances is mistaken for tuberculosis and can be distinguished from it only with difficulty This difficulty is increased by the fact that the two diseases are often combined Points that are sometimes helpful in differentiation are (1) The constitutional symptoms characteristic of tuberculous disease may not be so severe in fungus infections (2) In fungus infections the progress of the disease is sometimes extremely slow and is marked by the development of extraordinary fibrosis (3) Tuberculosis lesions in adults nearly always involve one or both upper lobes Pulmonary disease involving only the lower part of the lungs is seldom tuberculous Since fungi frequently cause lesions near the hilum or in the lower lobes the location of the disease is sometimes an important help in diagnosis

It is possible that immunity reactions may come to play a part in diagnosis For sporothrix and streptothrix agglutination and complement fixation tests have been devised and for sporothrix a subcutaneous and intracutaneous hypersensitiveness test similar to the tuberculin reaction These tests are not specific for a given variety of fungus but react to other allied micro organisms They may turn out to be of value in determining that invasion has actually occurred when fungi are found *in the sputum*

Finally the roentgen ray may give highly suggestive evidence For the most part the roentgenologist will diagnose fungus disease of the lungs as tuberculosis Dr F H Baetjer has said that he never felt sufficiently confident to make a definite diagnosis of pneumonomycosis from the roentgen ray plate alone Certain pictures however interpreted in the light of the history and other clinical findings are highly suggestive There are three such pictures (1) A dense shadow with irregular margins and radiating bands situated near the hilum and without the surrounding soft shadows usually seen in tuberculosis (2) Scattered small clearly defined shadows sometimes with sometimes without one or more larger dense shadows (In the case of streptothricosis reported by Glaser and Hart there was a large dense shadow in the left upper lobe and numerous clearly defined shadows some as large as a cherry scattered throughout the right lung At autopsy these shadows corresponded with small abscesses) (3) A dense mottling of one or both lungs with numerous small shadows resembling the picture of acute disseminated miliary tuberculosis

Actinomycosis

The first recorded case of pulmonary actinomycosis was described by James Israel in 1878 Bollinger had described the disease in animals a year earlier, and since that time it has come to be known as the most common and widespread of the mycoces The causative agent is the actinomyces group, the commonest form being actinomyces bovis, which is the organism chiefly encountered in diseased cattle Of clinical actinomyces infections 90 per cent are probably due to this organism the remaining 10 per cent to the variety known as Nocardia It is impossible to differentiate between the clinical conditions and the symptoms alone The differentiation must be made by the isolation of the causative fungus in the laboratory Recent studies have shown that the source of infection is probably in the patient s mouth As in pulmonary abscess, poor dental hygiene is very likely a predisposing factor Pathogenic fungi however have been found in the tonsils and in the gums of apparently normal individuals and may conceivably serve as a source of infection Perhaps this accounts for the frequency of infection about the jaws and in the cervical region and for frequent aspiration in the lungs initiating pulmonary infection

Pulmonary infections are usually basal and bilateral, but they may be unilateral and may occur in any part of the lung The lesion spreads by direct extension and early pleural adhesions are common Occasionally before the development of adhesions the pleural cavity may be invaded and massive pleural effusions may result The tendency to develop early adhesions however makes extension into the pleura the rule, so that the bone muscles and other soft tissues are usually invaded Fascial planes commonly offer no barrier The pulmonary lesions may be primary as stated from the aspiration of infected material from the mouth, or they may occur as metastatic infections by way of the blood stream from other lesions The early lesions may occur as areas of bronchopneumonia Later abscesses may form presenting all the manifestations of pulmonary abscess The chief characteristic that distinguishes these abscesses from other pulmonary abscesses is their tendency to extend directly through intervening tissues to the chest wall and lead to the formation of sinuses

Symptoms Early in the course of the disease the symptoms are those of mild pulmonary infection with cough, expectoration, and irregular fever As the disease progresses the lesions ulcerate and the sputum becomes purulent and frequently blood tinged At this stage a

dry pleurisy is common Much less common is the development of an effusion Farther along in the course of the disease the temperature which may have been low becomes high and spiking and is accompanied by dyspnea night sweats and prostration At this stage also the infection may extend not only outward into the chest wall but inward involving the heart and pericardium as well as other structures in the mediastinum The white count is usually elevated with a high percentage of polymorphonuclear leukocytes

Physical Signs Very early in the course of the disease there may be signs pointing to involvement of the chest wall Later retraction of the affected side absent or bronchial breathing and numerous coarse moist *rales* appear over the site of infection Large effusions simulate those seen in pulmonary tuberculosis The signs of pulmonary infection however accompanied by the presence of cutaneous abscesses or fistulae are most suggestive of actinomycosis

Roentgenogram Chest films of the early stages may show only small areas of bronchopneumonia similar to those seen in other diseases appearing most commonly and usually bilaterally in the lower lobes As the disease progresses however areas of rarefaction may appear and uniform areas of density occur along the chest wall or the interlobar septa indicating the development of pleuritis Massive areas of consolidation may suggest neoplasm Proliferative or destructive changes in the ribs are of course common

Diagnosis As stated above the diagnosis is suggested by the presence of a localized lesion usually involving one or both bases especially in the presence of cutaneous abscesses or sinuses and when accompanied by destructive lesions in the ribs that have been discovered by x ray In the final analysis however the diagnosis is established only by finding the typical sulphur granules with tangled masses of gram positive branching filaments in the sputum or abscess secretions Material taken from unopened subcutaneous abscesses should not only be examined directly for the ray fungus but should be cultured under both aerobic and anaerobic conditions It may be more difficult to obtain the fungus from abscesses or sinuses that have been opened previously In these cases however material can be obtained from as deep as possible or the gauze dressings may be examined when freshly removed The disease may be confused with tuberculosis especially in the presence of large pleural effusions The gummatous lesions of syphilis may be confusing as they recently were in a case at the University of California Hospital where diagnosis of actinomycosis was made only to be proved erroneous by

other manifestations of syphilis As has been stated the x ray appearance may simulate neoplasm All other fungus diseases must be ruled out

Prognosis The prognosis in actinomycosis is still grave but much less so than before the advent of modern treatment Early reports indicated that less than 25 per cent of full blown cases of pulmonary actinomycosis recovered Recent statistics indicate that the outlook from now on should be much better

Treatment The usual supportive measures employed in the treatment of pulmonary tuberculosis should be used in cases of actinomycosis namely a liberal diet including adequate amounts of proteins and fruit juices with the addition of cod liver oil or other vitamin preparations Postassium iodide is probably of value administered orally in a saturated solution, 3 drops t i d increasing to 20 drops t i d has been recommended or it may be used in larger doses—for example, 10 to 40 drops t i d from the beginning If the patient tolerates the drug well, much larger doses at times appear to be of benefit Sodium iodide 1 gm intravenously per day has been recommended also especially in patients who cannot take the drug by month The use of sulfonamides was introduced by Walker[319] The usual doses of sulfadiazine are now recommended, although sulfamirazine may be substituted if desired Penicillin in doses of 100,000 to 500 000 units per day often produces marked clinical improvement In the judgment of Dobson and Cutting,[312] among others, it is believed that the combination of sulfadiazine and penicillin is more effective than the use of either alone In a report by Donald R Nichols and Wallace L Herrell[316] of the Mayo Clinic, five of nine patients treated with 80 000 to 1,000 000 units of penicillin daily recovered—a recovery rate of 56 per cent Before this series but after 1940 of 13 other patients with pulmonary actinomycosis who were treated without the use of penicillin 1- died Certain cases have been benefited by chloromycetin and others by aureomycin The antibiotic chosen should be determined by sensitivity tests on sputum using both aerobic and anaerobic cultures Certainly therapy should be contained for at least a month after the subsidence of symptoms and close follow up should be continued for many months after discharge Surgical drainage of the abscesses and sinuses is of course usually indicated All sinus tracts should be explored and the chronically infected tissue removed Where a great destruction of pulmonary tissue has occurred lobectomy and pneumonectomy probably offer the best chance of recovery, in conjunction with the measure described above

Blastomycosis

North American Blastomycosis

This disease is often referred to as Gilchrist s disease because it was described by him in 1894 Martin and Smith [33] have recently collected 374 cases including 3 of their own which they have reported together with a review of the literature The North American form of the disease is widespread having been reported from 28 states in the United States Smith[34] remarks that he has seen over 40 cases in North Carolina in the past 14 years It is not limited to the United States however occasional cases having been reported from Canada and England

Blastomycosis occurs chiefly in those who have contact with cattle such as farmers stock growers and to a less extent workers in stock yards The organism involved in the blastomyces dermatitidis which is a large double contoured highly refractive budding yeast like organism found in the sputum and secretions from the lesions The fungus appears as a white mold with an abundant mycelium when grown on Sabouraud s medium The European form grows as yeast like fungus in culture but budding forms are present in tissue in both varieties To avoid confusion David Smith[34] prefers to call the European form cryptococcosis or Torula infection Blastomycosis may occur at any age from infancy to senility but is most common between the ages of twenty and forty Smith states that the disease is nine times as frequent in males as in females All races are susceptible Although the disease is a general one involving the bones especially the vertebrae and ribs more commonly involved are the liver spleen and kidneys the nervous system the prostate gland and the lungs according to Smith who recorded 95 per cent of pulmonary involvement

Symptoms The onset is insidious the early symptoms usually being referred to the chest A dry cough slight chest pain mild fever and dyspnea are common initial symptoms Mild symptoms of this character may last for weeks or months With ulceration the sputum becomes purulent and may be blood streaked As the pulmonary lesions grow more extensive dyspnea becomes a more prominent feature of the disease and a spiking fever may appear together with night sweats and prostration as in actinomycosis The pleura may be traversed by the infection and sinuses may appear in the chest wall or the deeper structures of the mediastinum may be involved with lesions in the heart and

pericardium Ultimately of course, widespread dissemination occurs, with involvement of the other organs previously mentioned

Physical signs are similar to those enumerated under actinomycosis pulmonary abscess or advanced tuberculosis Nothing in the physical signs is diagnostic Early in the course of the disease an enlargement of the root shadows and linear markings may be the only change noticed Later a dense homogeneous mass may be seen often triangular in form continuous with and parallel to the hilus Areas of rarefaction are uncommon In miliary blastomycosis the film resembles that seen in exudative miliary tuberculosis While the solid lesions frequently simulate tumor cavitation is seen much less frequently than in either tuberculosis or coccidioidomycosis

There is an increased sedimentation rate and white blood count and a rise in the polymorphonuclear leukocytes

A positive skin test to blastomycis vaccine is usually present in pulmonary and systemic cases although as in the tuberculin test this is lost in the final stages A complement-fixation test has been employed by Donald S Martin which is said to be reliable in active progressive disease and to disappear with recovery False positives are said not to occur

Diagnosis is usually established by demonstration of the typical organisms either in the sputum or in pus from subcutaneous lesions Cultures should be made either on Sabouraud s medium or on meat infusion blood agar incubated at 37 C The yeast-like budding double contoured organism grows slowly on blood agar and develops small wrinkled wavy colonies after two or three weeks On Sabouraud's medium on the other hand the fungus, grown at room temperature develops in two to three weeks a white cottony aerial growth that darkens on aging

As in the case of actinomycosis the disease may be confused with all other fungus infections as well as with tuberculosis neoplasm lung abscess sarcoidodis and syphilis

Prognosis Martin and Smith[3, 73] state that the mortality rate may be as high as 92 per cent in patients who have been followed for two years or longer Smith believes that the prognosis is best in the hypersensitive patient without complement fixing antibodies in the serum In general the prognosis is not good regardless of the type of disease or the treatment administered

Treatment Bed rest and liberal diet supplemented by vitamins or cod liver oil are as important here as they are in tuberculosis or other

fungus infections They should be continued for some time after the temperature has become normal and certainly until the x ray lesions have shown an indication of resolution Iodides are usually recommended as in actinomycosis but Martin and Smith[323] have pointed out that patients who are hypersensitive to the blastomycis vaccine become worse with iodide therapy They believe therefore that if iodides are to be used the patient should first be desensitized to blastomycis vaccine Smith[324] suggests that if the vaccine shows an erythematous zone of over 2 cm in diameter it should be diluted 1 100 before being administered subcutaneously If the reaction is as large as 3 cm 1 1000 dilution should be used if still larger 1 10 000 Subcutaneous injections should consist of 1 cc of the indicated dilution increasing by 1 every other day until 1 cc is injected The next higher dilution used in a similar manner until the undiluted vaccine is administered Severe local or general reactions should not be produced If these occur desensitization should be repeated with smaller doses usually one tenth the dose that produced the reaction Following desensitization Smith begins treatment with iodides Cautiously increasing 1 drop a day up to a maximum of 20 drops t i d he then reduces the dose to 3 drops t i d and increases again to 0 On the other hand if the skin test is not positive iodides may be administered in any dose desired or sodium iodide may be given intravenously in 1 gm doses

Surgical drainage is indicated in the presence of pus in this disease as well as in actinomycosis Small doses of x ray are said to be helpful but probably should not be given to the hypersensitive patient until he has been desensitized

Stilbamidine is recommended in the following doses After one or more liver function tests establish the fact that the liver is not diseased 0 mg of 2 hydroxy stilbamidine is given in 100 cc of physiological saline administered by intravenous drip over a period of 1 hour If there is no untoward reaction the following day 100 mg may be given and repeated on the next day The fourth dose may be 200 mg in 200 to 300 cc of physiological saline which is repeated on the following day On the sixth day the dose may be 300 mg in 200 to 300 cc of physiological saline administered as before over a period of about 2 hours This does may be continued 3 to 4 weeks Smith states the patients improve slowly with this treatment and there is more improvement in the 3 months following this treatment than in the actual administration of this drug He points out that the drug accumulates in the body particularly in the skin and that the patient may have skin eruptions

when exposed to sunlight This however, can be controlled with pyribenzamine

South American Blastomycosis

The so-called South American blastomycosis involves the lungs much less frequently than the North American type It often occurs in workers on coffee plantations De Almeida[3] has reviewed and analyzed 570 cases Males are affected more frequently than females The highest incidence is between the ages of 20 and 30 These manifestations generally occur late in the course of the disease and like those in the North American type are characterized by cough and purulent sputum that is blood-streaked The lesion is much more likely to be diffuse suggesting hematogenous dissemination The physical signs therefore are more likely to be present throughout both lungs and the x ray evidence to consist in patchy infiltration scattered throughout both lung fields Cavitation may occur

The *treatment* is the same as that for the North American type although sulfonamides have been said to bring about dramatic improvement in the condition

Cryptococcosis (European Blastomycosis)

Cryptococcosis caused by the fungus Cryptococcus neoformans frequently involves the lung but also results in lesions of the skin brain meninges and other parts of the body It is found in all parts of the world Formerly called torulosis after the old name for the infecting fungus Torula histolytica it is now known in Europe as Buss Buschke s disease or blastomycosis and in America as European blastomycosis

No age appears to be exempt although most of the recorded cases have involved adults between forty and sixty years of ages Males appear to be slightly more affected than females Non pathogenic strains of cryptococci as well as a certain number that were pathogenic for animals have been isolated from the skin of normal individuals by Benham[320] Pathogenic strains have also been isolated from naturally occurring infections in animals as well as from fermenting fruit juices

Symptoms The onset is usually insidious with an irritative cough and a small amount of mucoid sputum that may later become blood

streaked Fever if present is usually low grade except in severe infections The physical signs in mild cases may consist in wheezing on one or both sides In more advanced lesions characterized by consolidation the usual signs of a localized pneumonitis may be present The signs may persist after symptoms of acute infection have disappeared or in the course of the disease the signs of meningitis may appear as the infection spreads to the brain or meninges With terminal generalized dissemination *rales* may appear throughout both lungs

Roentgenogram Large localized shadows that resemble a tuberculoma or alveolar cell carcinoma may occur anywhere in the lung fields Cavitation in these lesions is uncommon The enlargement of the mediastinal nodes is also uncommon With terminal dissemination the picture may resemble that seen in miliary tuberculosis

Diagnosis Since the pulmonary symptoms and x ray films are not to be distinguished from other pulmonary fungus infections the diagnosis of primary pulmonary cryptococcosis must be made from cultures of the sputum on Sabouraud s medium The colonies appear soft creamy white and mucoid and when smears are made with India ink the budding yeast cells can be seen surrounded by a relatively large capsule The complement fixation test in this disease is unreliable According to Benham[849] the injection of whole yeast cells produces no demonstrable agglutinins or precipitins in rabbits He did find however that if he removed the capsule demonstrable antibodies were present Vaccines have been used in the hope of producing positive skin tests but so far have proved unreliable

The disease is to be differentiated from other types of bronchitis and other mycotic infections as well as from tuberculosis which it sometimes closely resembles

Prognosis Many unrecognized mild cases must have occurred with spontaneous recovery Most of the recorded cases of primary pulmonary infections however have resulted in death from widespread infections involving the brain and meninges

Treatment The treatment is symptomatic and supportive as described under other fungus infections David Smith[823] reports the treatment of two cases with sulfadiazine in doses sufficient to maintain a blood level of 8 to 12 mg per 100 cc of blood and recommends that the drug be continued for several weeks after the disappearance of symptoms One patient was clinically well two years after the treatment was stopped the other developed sensitivity to the drug and later died from a spread of the disease to the brain Another cure with sul

when exposed to sunlight This, however, can be controlled with pyrabenzamine

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Symptoms The onset is usually insidious with an irritative cough and a small amount of mucoid sputum that may later become blood

be demonstrated on culture Unlike tuberculosis however the primary form of the disease is frequently complicated by spontaneous pneumothorax hydropneumothorax and pulmonary cavitation

Coccidioides immitis has been shown to be present in the soil of the arid regions of the southwest Consequently most primary infections in men and animals occur during the dusty seasons Rodents in endemic areas are susceptible as are cattle sheep and dogs but cross infections from animal to man or from man to man seldom if ever occur

Symptoms An excellent opportunity for study was afforded by the accumulation of large numbers of previously uninfected individuals in endemic areas during World War II A group of 75 soldiers with primary coccidioidomycosis was reported by Goldstein and MacDonald[340] In these soldiers the incubation period varied from one to three weeks The great majority of the patients complained of cough pain in the chest and fever, 18 per cent had hemoptysis Only one quarter of the patients presented abnormal physical signs and these were limited to alteration of breath sounds *Rales* were seldom found Erythema nodosum developed in 19 per cent of these cases erythema multiforme in 6 per cent and a morbilliform rash over the trunk and lower extremities in 4 per cent The skin lesions occurred 8 to 14 days after the onset of symptoms and were usually accompanied by eosinophilia this leads to the conclusion that they were probably allergic in nature Pleurisy with effusion occurred at the same time in a few cases

Roentgen Appearance Colburn[335] compiled the roentgen findings of the 75 soldiers reported by Goldstein and MacDonald[340] Four per cent showed no abnormal x ray changes 38 7 per cent however showed fan shaped densities in conjunction with enlarged hilar lymph nodes The parenchymal densities resolved in from 15 to 90 days In roughly one quarter of the cases enlarged hilar lymph nodes were present without parenchymal lesions In another quarter there were peripheral infiltrations in either the upper or the lower lobes The thin walled cavity so characteristic of pulmonary coccidioidomycosis occurred in only 4 per cent Some of these cavities healed in from 60 to 95 days while others persisted Indeed cavities of this nature have been known to persist for from 5 to 10 years without impairing the health of the patient As primary infections heal calcification may occur in the periphery of the lung or in the hilar lymph nodes exactly as they occur in pulmonary tuberculosis or in histoplasmosis Calcified lesions that are healing however have been shown to harbor Coccidioides immitis for many years after the clinical infection has died out

fadiazine has been reported by Marshall and Teed Penicillin apparently has no effect on the infection and iodides appear to be without benefit

Coccidioidomycosis

This disease was first reported from South America in 189 by Posadas and Wernicke The first recorded case in the United States was that of Rixford, who in 1894 reported a patient from the San Joaquin Valley of California with a severe generalized fatal infection Ophuls and Moffitt[341] gave the first adequate clinical description of the disease For many years the severe disseminated type was the only form recognized, until Gifford and Dixon in 1935 established the connection between the so-called valley fever and what was then called coccidioidal granuloma Recognizing the identity of the etiological agent, Dickson[339] of Stanford University proposed the term primary and secondary coccidioidomycosis to designate the two types Subsequently, Charles E Smith[341] also of Stanford contributed extensively to our understanding of this disease It is now generally recognized largely because of his work that human infections with Coccidioidos immitis are usually acquired by inhaling the clamydospores and arthrospores of the fungus The lungs therefore are the usual portal of entry, but abrasions or lacerations of the skin may also serve as initial sites of development Smith states that three fifths of the infections are completely asymptomatic Those patients who do show symptoms, however, usually do so after an incubation period of one to three weeks with respiratory symptoms of varying severity

Primary Coccidioidomycosis The pathogenesis of coccidioidomycosis resembles that of tuberculosis The fact that most primary infections pass unrecognized is a strikingly similarity The symptoms of a primary infection are usually those of a cold or grippe with low grade fever for a few days and a non productive cough In the San Joaquin Valley of California this manifestation is called valley fever Erythema nodosum is a frequent complication leading to the designation of 'the bumps According to Smith[341] this occurs in 4 per cent of all coccidioidal infections of white males and in 20 per cent of cases of clinically manifest disease It is higher in adult females, appearing in 10 to 25 per cent of their infections and in 40 per cent of their clinically manifest disease As in tuberculosis pleural effusion is common and occurs soon after primary infection The fluid is serous, and the fungus can usually

be demonstrated on culture. Unlike tuberculosis, however, the primary form of the disease is frequently complicated by spontaneous pneumothorax, hydropneumothorax, and pulmonary cavitation.

Coccidioides immitis has been shown to be present in the soil of the arid regions of the southwest. Consequently most primary infections in men and animals occur during the dusty seasons. Rodents in endemic areas are susceptible, as are cattle, sheep, and dogs, but cross infections from animal to man or from man to man seldom if ever occur.

Symptoms. An excellent opportunity for study was afforded by the accumulation of large numbers of previously uninfected individuals in endemic areas during World War II. A group of 75 soldiers with primary coccidioidomycosis was reported by Goldstein and MacDonald.[310] In these soldiers the incubation period varied from one to three weeks. The great majority of the patients complained of cough, pain in the chest, and fever; 18 per cent had hemoptysis. Only one quarter of the patients presented abnormal physical signs and these were limited to alteration of breath sounds. *Rales* were seldom found. Erythema nodosum developed in 19 per cent of these cases, erythema multiforme in 6 per cent, and a morbilliform rash over the trunk and lower extremities in 4 per cent. The skin lesions occurred 8 to 14 days after the onset of symptoms and were usually accompanied by eosinophilia; this leads to the conclusion that they were probably allergic in nature. Pleurisy with effusion occurred at the same time in a few cases.

Roentgen Appearance. Colburn[75] compiled the roentgen findings of the 75 soldiers reported by Goldstein and MacDonald.[310] Four per cent showed no abnormal x-ray changes; 38.7 per cent, however, showed fan-shaped densities in conjunction with enlarged hilar lymph nodes. The parenchymal densities resolved in from 15 to 90 days. In roughly one quarter of the cases enlarged hilar lymph nodes were present without parenchymal lesions. In another quarter there were peripheral infiltrations in either the upper or the lower lobes. The thin-walled cavity so characteristic of pulmonary coccidioidomycosis occurred in only 4 per cent. Some of these cavities healed in from 60 to 95 days, while others persisted. Indeed, cavities of this nature have been known to persist for from 5 to 10 years without impairing the health of the patient. As primary infections heal, calcification may occur in the periphery of the lung or in the hilar lymph nodes exactly as they occur in pulmonary tuberculosis or in histoplasmosis. Calcified lesions that are healing, however, have been shown to harbor Coccidioides immitis for many years after the clinical infection has died out.

As in tuberculosis the primary form of the disease may become progressive In the presence of continued fever and a spreading lesion discovered by x ray or in the presence of metastatic lesions in other parts of the body, the diagnosis of progression is inescapable These instances may rapidly proceed to a fatal termination In this stage a miliary spread of the disease may occur accompanied by meningitis

Coccidioidal Granuloma (Secondary Coccidioidal Infection) More commonly coccidioidal granuloma or disseminated progressive or secondary coccidioidal infection occurs *di nuovo* in patients in whom the primary valley fever stage of the disease passed unrecognized The manifestations are severe, progressive pulmonary lesions with extra pulmonary lesions of the lymph nodes, bones joints central system peritoneum genital tract skin mucous membranes of the mouth and so forth In this respect the disease also parallels tuberculosis Fifty per cent of these patients still die

Symptoms and Signs Studies made during World War II show that among white adult males one in 380 of those infected and one in 100 with clinical disease manifest extrapulmonary dissemination Negroes appear to be more susceptible than whites, the risk of dissemination being increased at least ten times Apparently dissemination occurs soon after infection According to Smith[311] dissemination is usually a matter of weeks seldom a matter of years Here again it is likely that the analogy with tuberculosis is marked This fact however has led Smith to the conclusion that the great difference between tuberculosis and coccidioidal infection lies in the fact that coccidioidal pulmonary cavitation is not in the category of disseminating or progressive coccidioidal granuloma The tendency of early coccidioidal infection to develop cavities is certainly in striking contrast to primary pulmonary tuberculosis although it is well known that cavitation may occur in the latter Smith[311] reports coccidioidal cavities appearing within a week or two after the onset of a pneumonic lesion As far as dissemination is concerned however such cavities appear to be innocuous Nevertheless Reginald Smart has reported spread from coccidioidal cavities including one patient who died of coccidioidal meningitis

Diagnosis In or near endemic areas acute febrile illnesses with respiratory symptoms or chronic pulmonary lesions with or without cavitation usually raise a question of possible infection with coccidioides immitis The first step in the diagnosis is the application of a coccidioidin skin test The material is made from a filtrate of synthetic asparagin broth culture as described by Smith[314] There need be no fear that

dissemination may occur as a result of the test or that it will alter the precipitant or complement fixing antibodies Reactions to histoplasmin however may be confusing especially when concentrations greater than 1 100 are used Occasionally the skin test will be negative when the disease is known to be present Smith stated that in his series one sixth of the patients did not react to 1 100 coccidioidin Most of those who did not react to 1 100 dilution however were positive on the 1 10 dilution Even so 3 per cent of the culture positive diagnostic group were stated to be negative to 1 10 coccidioidin Readings of coccidioidin skin tests should be made at 24 and 48 hours Induration over 5 mm should be read as positive at either period according to Smith In all probability the coccidioidin skin test in skilled hands is about as reliable as the tuberculin test

In the hands of Charles Smith[314] both precipitin and complement fixation tests have been found to be of great value in diagnosis Both tests are generally negative in mild coccidioidal infections and positive in more severe infections Smith states that the precipitins appear before complement fixing antibodies but that the latter persist longer Precipitins are found only within the first month or two after the infection has been acquired and have thus vanished by the time most cavities appear In a group of 107 patients with pulmonary cavitation the sera of approximately three fifths of the culture positive group fixed complement to a diagnostic titer only one quarter were negative In progressive coccidioidomycosis complement fixing antibodies are present in a high titer

Sputum and exudates should be examined directly with the use of 10 per cent sodium hydroxide to detect the typical spherules These are large thick walled structures o to 80 mu in diameter containing numerous small endospores to 5 mu in diameter They are doubly refractive Sputum and other secretions should also be planted on Sabouraud s medium and incubated at room temperature As a rule growth will develop within two weeks in the form of a moist colony on the surface of the medium As incubation is continued a cottony aerial mycelium appears which is at first white but later darkens This material is very fluffy Great care should be exercised in inspecting the colonies after the growth has matured since numerous laboratory infections have been reported These infections have occurred as a result of the inhalation of the thick walled rectangular or spherical arthrospores which are 3 to 4 mu in size

Differential Diagnosis Primary coccidioidomycosis must be differentiated from the common cold influenza bronchial pneumonia or

primary atypical pneumonia Coccidioidal granuloma must be differentiated from tuberculosis, tularemia neoplasms, and especially from other mycoses particularly blastomycosis and actinomycosis

Prognosis The prognosis is excellent in primary pulmonary coccidioidomycosis although residual cavities may persist for months or years In progressive coccidioidomycosis the prognosis is graver, the mortality is over 50 per cent

Treatment Acute primary coccidioidomycosis should be treated like any other febrile illness by rest in bed and an adequate diet It is doubtful if treatment need be continued beyond the febrile period unless cavitation persists Since there is probably no transference from man to man there is no public-health aspect to the disease as in tuberculosis Coccidioidal granuloma requires rest in bed and a high caloric diet supplemented by vitamins and if the coccidioidal areas is limited in extent excision may be considered Recently isolated coccidioidal cavities have been treated by direct excision of the cavity itself Under the supervision of Dr W L Rogers[343] and others this has been proved to be uniformly successful Apparently dissemination need not be feared Pneumothorax has been used in the treatment of such cavities as has the crushing and the phrenic nerve or pneumoperitoneum It is doubtful however if any surgical measure is as satisfactory as excision

2-Hydroxy-stilbamidine is recommended as specific therapy and should be used in the same manner as it is for blastomycosis In all probability this treatment is not necessary in primary cases and should be reserved for the granuloma type of the disease

Geotrichosis

This infection seldom recognized clinically usually produces a mild bronchitis rather than a severe pulmonary ailment like those produced by blastomycosis Normal individuals may harbor the fungus in their mouths or intestinal tracts Consequently, mild mouth and intestinal infections are common In appearance the organism may be confused with Blastomyces dermatitidis Direct examination of secretions especially sputum is essential because of the presence of geotrichum in the oral cavities of normal individuals The sputum should be treated with a drop of 10 per cent sodium or potassium hydroxide and examined directly under the microscope The fungus then appears as cells 4 to 8 mu in diameter with somewhat rounded ends, or as

large spherical cells 4 to 10 mu in diameter The fungus grows on Sabouraud s glucose agar at 37 C or at room temperature In the latter case the growth extends down into the medium and the long hyphae break up into rectangular arthrospores The presence of these rectangular arthrospores establishes the diagnosis of geotrichosis At 37 C the colony is to a great extent confined to the surface of the medium

Symptoms This disease occurs most frequently as a mild bronchial infection with cough and the expectoration of a peculiar mucoid or gelatinous sputum that is rarely blood streaked The patient complains chiefly of cough and general symptoms are lacking Physical examination usually reveals *rales* at both bases and the roentgen films may show linear accentuation at the bases or fine mottling extending into the mid lung fields A more severe form of the disease invades the lungs with the production of systemic symptoms There may be elevation of temperature pulse and respiration and the leukocyte count may be increased The sputum is largely mucoid however but may contain blood and frank hemoptysis may occur From the sputum organisms can easily be cultured on Sabouraud s medium

Physical examination reveals dullness and bronchovesicular breathing with fine or moderately coarse *rales* over the involved area *Roentgen examination* reveals patchy infiltration and occasionally small thin walled cavities When the lesions occur in the upper lobes they can easily be confused with pulmonary tuberculosis of an exudative character

David Smith[39] has found geotrichum in association with Friedlander s bacillus as well as with tubercle bacilli and in these cases he has been uncertain of the importance to be attached to the presence of geotrichum

Treatment is the same as for other fungus infections The mild bronchial form of the disease responds readily to treatment with potassium iodide in large doses

Histoplasmosis

Since the middle thirties scattered cases of a disease caused by Histoplasma capsulatum have been reported in the literature At first it was thought to be a serious almost uniformly progressive disease leading to death but it has recently been demonstrated that most infections are mild and clinically unrecognizable This has been shown by the painstaking studies of Carroll Palmer Michael Furcolow and

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with circumscribed soft infiltrates have been asymptomatic In the more advanced cases that have been reported cough and expectoration were early symptoms while in severe infections emaciation and aenemia became prominent A marked leukopenia has been reported Adenopathy other than of the hilus lymph nodes has been associated with splenomegaly and hepatomegaly Ulcerations in the nasal oral and pharyngeal cavities have been discovered When severe localized pulmonary infections were described dullness changes in breath sounds and *rales* occurred over the involved areas

Roentgenogram The most prominent feature of the roentgenogram has been the extensive calcification both in the lung and in the hilus lymph node Nodular foci and pneumonic infiltrations are not uncommon These may resemble disseminated tuberculosis Excellent roentgen illustrations appear in Public Health reports for 4 November 1949

Diagnosis If the histoplasmin skin test is positive a negative tuberculin reaction is of help The final diagnosis depends on the isolation of Histoplasma capsulatum from the sputum or tissue The disease is to be differentiated from tuberculosis and from other fungus infections

Treatment No worth while specific treatment has so far been recorded During the acute phases of severe infections rest in bed with an adequate high calorie diet reinforced by the addition of vitamins should be of benefit The relief of pain should be accomplished by measures that do not interfere too much with the cough reflex Whether the early infiltrates clear more readily with bed rest is not known

Mold Infections

Aspergillus penicillium and mucor are widely distributed in nature They may at times cause primary disease but are found more commonly as secondary invaders in patients with tuberculosis bronchiectasis or bronchogenic carcinoma External ear infections with aspergillus are common The skin nasal sinuses bronchi and lungs are also involved as are occasionally the bones and meninges French workers have reported many cases of aspergillus infections occurring in squab feeders who take grain into their own mouths and thus inhale spores in fur renovaters who use rye flour and may inhale dust containing spores and in threshers who commonly inhale large numbers of spores Numerous cases have been reported from England Australia North and

others connected with the United States Public Health Service In the United States the disease has been shown to be most common in Missouri Tennessee, and other southern states as well as in Michigan, Illinois and Ohio In general the Mississippi and Missouri River valleys are endemic areas The disease has also been reported from Central and South America and the Philippines as well as from England and South Africa All races and ages are affected Calcification of the lungs and hilus lymph nodes is common in children in the endemic areas Presumably it is caused by past infections with Histoplasma capsulatum since the tuberculin reactions were negative and the affected individuals reacted to histoplasmin

Unlike sporotrichum and monilia, Histoplasma capsulatum has not been found in nature The organism may be found in smears stained with Wright's or Giemsa's stain in the form of small oval yeast like cells in the macrophages Cultures on Sabouraud's medium grown at room temperature for several weeks reveal large tuberculate chlamydospores characteristic of the mycelial phase

The development of our knowledge of histoplasmosis closely parallels that of coccidioidomycosis In both instances the disease was at first thought to be uniformly fatal for the cases reported in the early literature were serious advanced examples of the disease Both are now recognized to occur most commonly in a mild form resembling primary tuberculosis The initial lesion is presumably in the lung with rapid extension to the hilar lymph nodes Calcification in both lung and lymph node seems to be more common in infections with Histoplasma capsulatum than in infections with the tubercle bacillus, or Coccidioides immitis In histoplasmosis widespread uniform calcification of the pulmonary parenchyma occur presumably due to post-primary miliary dissemination of a benign type In a study of 3 105 student nurses Carroll Palmer[350, 351] found pulmonary calcifications more common among those who were positive to histoplasmin and negative to tuberculin than among those who were positive to tuberculin but negative to histoplasmin Christie and Peterson[352] obtained the same findings in Tennessee children and the recent study by Furcolow, High, and Allen[350] in Kansas City Missouri produced a similar result also Pulmonary calcifications were approximately twice as frequent among those who were histoplasmin positive and tuberculin negative as among those who were tuberculin positive and histoplasmin negative

Symptoms Most of the cases of pulmonary calcification, even those

with circumscribed soft infiltrates have been asymptomatic In the more advanced cases that have been reported cough and expectoration were early symptoms while in severe infections emaciation and aenemia became prominent A marked leukopenia has been reported Adenopathy other than of the hilus lymph nodes has been associated with splenomegaly and hepatomegaly *Ulcerations in the nasal oral* and pharyngeal cavities have been discovered When severe *localized* pulmonary infections were described dullness changes in breath sounds and *rales* occurred over the involved areas

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South America and the southern European continent Mold infections have been reported as a frequent cause of intrinsic asthma in Low Countries In these cases positive skin tests have been thought to be significant

Symptoms Mold infections produce cough with mucoid or mucopurulent sputum not infrequently tinged with blood The general health may or may not be affected In some cases there is malaise, intermittent fever anorexia with loss of weight and consequent cachexia This slow downhill course is strikingly similar to that seen in pulmonary tuberculosis

Roentgenogram Smooth patchy shadows in one or both lungs appear in the roentgenogram but are not diagnostic, being similar to those seen in fungus infections Cavitation is not uncommon

Diagnosis Cultivation of the fungus from the sputum is not sufficient for diagnosis since the organisms occur so frequently as secondary invaders When other conditions have been ruled out, however and when branching hyphae have been repeatedly demonstrated in the sputum, the diagnosis of primary infection with aspergillus, penicillium or mucor is justified Tuberculosis and other mycoses must be excluded

Prognosis As a rule the prognosis is favorable Where there is massive involvement of the pulmonary tissue, however especially where extensive cavitation is present the prognosis is grave

Treatment Bed rest with a liberal high calorie diet is indicated until the x ray is cleared Potassium iodide in the usual dosage or up to the patient s limit of tolerance may be useful If skin tests show that the patient is very hypersensitive to the invading organism he should be desensitized before iodides are administered or the latter should be given cautiously in the beginning

Moniliasis

Moniliasis is caused by a fungus known as monilia or Candida albicans which is one of the fungi found normally inhabiting the mouth and skin Pathogenic species however have been found to produce lesions on the skin above the nail beds in the mouth vagina bronchi and lungs, and more rarely a widespread septicemic infection with endocarditis and at times meningitis The organism is a budding yeast-like fungus growing readily on Sabouraud s medium Since saprophytic forms are so widespread however it is always necessary,

where this disease is suspected to prove that the isolated fungus is in fact pathogenic and not a secondary invader

Lesions in bronchopulmonary moniliasis may involve the bronchi alone or extend into the parenchyma of the lungs producing broncho pneumonic or pneumonic lesions that affect part of a lobe an entire lobe or a lung At times some lobes may show complete consolidation while others contain bronchopneumonic patches Such lesions may clear rapidly to be followed by fresh lesions involving other parts of the lungs

Symptoms The onset in the bronchopulmonary form of the in fection is usually insidious and characterized by cough with a small amount of clear mucoid sputum If carefully searched for the sputum even at this stage may be found to contain small gray flakes that contain a budding fungus mixed with cellular debris In such cases there may be no other symptoms The patient may feel perfectly well except for the distressing cough Such lesions may clear spontaneously but as a rule the disease is characterized by remissions with a recur rence of symptoms after both the patient and the doctor believe that the disease has been cured With each exacerbation wheezing and moderately coarse *rales* at one or both bases may be found on physical examination When fever occurs it is usually found that the disease involves the parenchyma of the lung In these cases pleuritis is common with or without effusion the cough becomes markedly increased and troublesome and the sputum may become blood streaked When secondary infection is marked the sputum is frankly purulent With the usual bronchopneumonic type of infection the physical signs are similar to those found in other types of bronchopneumonia In the presence of lobar consolidation the signs are those of lobar pneumonia with flatness increased tactile fremitus increase in whispered voice bronchial breathing and consonating rales

Roentgenogram In the bronchial form of the disease there is a generalized increase in linear markings otherwise the shadows resemble bronchopneumonia and are confluent or poorly defined In severe cases the complete consolidation of one or more lobes may be demon strated It is characteristic of the disease that the x ray shadows clear rapidly only to recur elsewhere in the lung fields

Diagnosis The sputum should be cultured on Sabouraud s medium although the fungus can sometimes be found by direct examination of the sputum Animal innoculation is necessary in order to prove patho

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out the world the organism growing as a saprophyte on plants and causing spontaneous infections in a wide variety of both wild and domestic animals Karl Meyer[109] recovered the fungus from the coats of healthy horses and infected himself from one of the cultures Sporotricha have also been found on the fur and in the mouths of apparently healthy rats Human infections have been reported to have come from handling contaminated dressings

In 1915 Karl Meyer[110] collected 400 cases of sporotrichosis from the literature Since that time many more have been added in only a few of which has pulmonary involvement been mentioned In the majority of reported cases however x ray findings have not been mentioned and it seems likely that if routine x ray studies of these cases had been made more pulmonary lesions would have been discovered

David Smith[111] lists 9 presumably authentic cases showing pulmonary manifestations of this disease including one from Duke Hospital in a child 10 years old who presented the picture of asthmatic bronchitis X ray films showed enlarged hilar lymph nodes although the child failed to react to an intradermal test with 1 mg of tuberculin Sporotrichum Schenkii was isolated from her sputum and her blood serum agglutinated a suspension of sporotrichum spores in a dilution of 1 1000 An autogenous vaccine gave an immediate skin reaction

Pulmonary Symptoms Since most of the recorded cases of sporotrichosis have occurred in association with other manifestations of the disease it is difficult to determine the mode of onset Dominguez reported malaise weakness loss of weight and fever In the case he studied there was copious sputum from which filaments of sporotrichum could be obtained This patient had been working with contaminated tobacco The same strain of organism had been isolated from this source

Roentgenogram Recorded pulmonary cases have usually shown rather marked enlargement of the hilar lymph nodes In some cases fine patchy infiltration has been present and in others areas of consolidation Cavitation has been recorded

Differential Diagnosis The disease must be differentiated from tuberculosis As in other fungus infections the failure to find tubercle bacilli in the sputum is suggestive In hilar lymph node involvement a negative tuberculin skin test with second strength P P D or 1 mg of old tuberculin is of great value Pyogenic infections are usually determined easily Tularemia syphilis glanders and leprosy must be ruled

genicity Agglutinins have been demonstrated in the sera in titers as high as 1 2400 Severe infections however may be present with no demonstrable agglutinins in the blood Skin reactions are unreliable since many normal individuals give positive reactions They are of great value however in determining the degree of hypersensitivity In all cases every effort should be made to rule out other causes for the pulmonary lesions since non pathogenic species of the fungus are so common Moniliasis must be differentiated from other types of bronchitis other mycoses and pyogenic infections

Prognosis Mild bronchial infections often heal spontaneously Mild recurring forms of the disease may last for years with exacerbations and remissions The pulmonary form of the disease usually clears up in from four to six weeks with adequate therapy

Treatment Large doses of potassium iodide are usually effective These are to be administered only after skin tests in which heat-killed vaccines have been used to determine the degree of sensitivity Hyper sensitive patients should be desensitized before administration of iodides

Sporotrichosis

Pulmonary sporotrichosis has until recently been thought to be a relatively rare form of infection from Sporotrichum Schenkii Much more common is infection of the lymph nodes skin and subcutaneous tissues with nodules and later abscess formation coinciding with the production of chronic ulcers

The causative organism appears on blood agar or on Sabouraud s dextrose agar slants as very small colonies that are white circular and silky in appearance Short mycelia penetrate the media but there are no aerial mycelia Campbell[v] has reported growth on Francis glucose cystine blood agar introduced for the cultivation of Pasteurella tularense In any case the tubes should be incubated at 37 C and also at room temperature and examined for the appearance of the fungus every four days although they should not be discarded in less than six weeks

The disease has been reported from infancy to old age but is most common in the thirties and forties David Smith[3r] states that about 10 per cent of the cases occur in children and that the disease is nine times as frequent in males as in females Farmers and laborers are most frequently affected All races appear to be susceptible

Like most other fungi Sporotrichum Schenkii is distributed through

it aroused a great deal of interest Apparently it can be introduced into uninfected flocks by sick animals and it is said that animals that merely occupy the quarters previously used by infected animals may them selves become ill In sheep both sexes and all ages appear to be sus ceptible

Case History A white married female 51 years of age was seen at the University of California Hospital in 1948 Her family history marital history and past history until eight or nine years ago seemed to be entirely non contributory except that in 1939 or 1940 her neigh bors had a small flock of sheep that fell ill with an acute type of pul monary infection from which many of the sheep died The patient s contact was casual involving an interest in the misfortune of her neighbors but not to the extent of any care of the sick animals At about this time however or shortly thereafter she noticed the ap pearance of a dry hacking cough that was irritative and non productive She believes that in 1941 or 194 she began to raise small amounts of clear mucoid frothy sputum and that at the same time her cough became rather more prominent She consulted a physician because of her pulmonary symptoms at this time Her physical examination was essentially negative but an x ray was said to show some abnormal findings in the region of the right lower lobe although the film was lost or misplaced and could not be obtained for comparison with sub sequent roentgenograms The diagnosis at this time was bronchiectasis involving the right lower lobe Meanwhile however her symptoms gradually became worse The sputum increased although it remained mucoid and frothy In 1944 her symptoms became still worse and a film of this date was also said to reveal a pathological process in the right lower lobe and bronchograms were said to show bronchiectasis In 1945 the cough became still more marked and the right lower lobe lesion again appeared in the x ray film This film dated 6 June 1945 revealed an area of increased density roughly triangular in shape lying just above the diaphragm and posterior to the interlobar septum between the right middle and lower lobes A bronchoscopic examina tion was essentially negative The symptoms continued to increase The sputum which up to this time had been glairy white mucus became thick yellow and foul smelling and the patient described a troublesome musty odor She was also troubled by vague right lower chest pain that was never pleuritic in character

A film taken in July 1946 revealed slight enlargement of the shadow

out Other types of fungus infection must be eliminated by culture of the fungus and by agglutination tests

Unfortunately, a positive culture of sporotrichum obtained from the sputum is insufficient for diagnosis, since the organism is known to occur in normal mouths as well as on vegetable material The patient s serum in a dilution of at least 1 50 should agglutinate the spores of sporotrichum grown from his own secretions The higher the dilution however the more likely the diagnosis

Prognosis While the outlook in the lymph node form of sporotrichosis is usually excellent visceral forms including the pulmonic, are malignant and have a poor prognosis

Treatment Potassium iodide in doses of 10 drops t i d of the saturated solution increasing to the patient s tolerance, is the only known treatment of value and appears to be specific for this infection Penicillin may be used to combat the secondary infection accompanying severe pulmonary involvement X ray has been suggested for indolent lesions

Pulmonary Alveolar Adenomatosis

In March 1945 David A Wood and Philip H Pierson[379] reported the first case of pulmonary alveolar adenomatosis in which the diagnosis had been made before death In this patient the diagnosis was established by a lobectomy performed by Dr Emile Holman six months before death

Pulmonary alveolar adenomatosis is said to be a rare disease in man, although a dozen authenticated cases have now been reported Among them are those of Lohlein[3 1] Sims[377] Obendorfer[3 4] Helly,[3] Bonne[370] Richardson,[3 6] Briese[3 1] Bell[369] Taft and Nickerson[3 8] and three additional cases reported by Paul and Ritchie[3 5] The etiology of the human disease is still in doubt and the pathogenesis is far from clear The disease is certainly rare but bears a remarkable resemblance to benign pulmonary adenomatosis which has been reported as occurring epizootically in the sheep of Iceland South Africa England and the United States, especially in certain areas of Montana The disease characteristically appears when sheep are being driven from place to place, hence the South African name jagsiekte or driving disease' In Montana it has apparently been called progressive pneumonia' The disease appeared for the first time in Iceland in 1934 and spread so rapidly that

flammatory cells are noted with early fibrosis of alveolar walls The bronchioles are somewhat dilated and often contain mucus At the margin of the more normal lung noted grossly the pulmonary parenchyma is compressed and the near by alveoli are distended with many large reticulo endothelial cells of finely granular cytoplasm There are large numbers of eosinophils and considerable intra alveolar bleeding The bronchioles and bronchi in this region are also compressed and the smaller blood vessels show perivascular cuffing with chronic inflammatory cells and eosinophils The pleura shows an increased number of chronic inflammatory cells The hilar lymph nodes show only moderate anthrocosis with a slight increase in the number of eosinophils

Diagnosis Pulmonary adenomatosis

Following lobectomy the patient made an uneventful recovery and up until the present time has remained perfectly well without a recurrence of any of her symptoms She has pursued her normal life without handicap

While this disease is rare, we are of the opinion that it may be somewhat more common than heretofore believed If as Wood and Pierson[3 9] apparently believed the disease is of true virus etiology, it is interesting to speculate upon the possible effect of some of the new antibiotics It is quite possible that opportunities may arise for their trial in the future since the disease is not always localized to one area of the lung but may appear simultaneously in different lobes

The case for virus etiology is still presumptive Certainly there is a definite similarity between the morphological appearance of human cases and ovine disease There is a strong case for the virus etiology of the latter for the transmission from animal to animal appears to be well recognized So far however there is no known recorded instance in which transmission has occurred from man to man

Is there any relationship between this disease and so called primary alveolar cell carcinoma of the lung? So far this question remains unanswered Certainly there are many points of similarity Nevertheless the paucity of the mitotic figures and the absence of stromal invasion are characteristic of pulmonary alveolar adenomatosis Apparently the hyperplasia of columnar epithelium is primary and stromal changes are secondary An excellent review of the disease as it occurs in Icelandic sheep may be found in Wood and Pierson's[3 9] article and is therefore not repeated here In the same article is an excellent discussion of the case for and against virus etiology

described in the film of a year earlier A year later, however, in July 1947 the antero-posterior film revealed a shadow that looked more extensive but nevertheless similar to the preceding ones although the latter film showed that the process behind the interlobar septum had apparently cleared The area of density now occupied a triangular region lying against the posterior chest wall, the area above the diaphragm being free A film taken on 15 December 1947 did not differ from the one taken in July of the same year

Examination of the blood showed the hemoglobin to be 101 per cent, red blood cells 4 970 000 white blood cells 14 150 polymorphonuclears 86 per cent eosinophils 1 per cent, basophils 0 per cent, lymphocytes 9 per cent and monocytes 4 per cent

Because of the rather casual previous exposure to sick sheep the long insidious illness to which no other etiology could be ascribed and the striking resemblance of the patient to the Wood and Pierson[59] case reported in 1945 a diagnosis of pulmonary alveolar adenomatosis was made Since no therapy had heretofore proved effective in this disease and since it appeared to be limited to the right lower lobe, right lower lobe lobectomy was agreed upon Accordingly on 4 May 1948 Dr H Brodie Stephens performed the operation by the individual ligation technique finding the right lower lobe quite free firm throughout, salmon pink in color and with a peculiar smooth, solidified surface The pathological report follows

Material from right lower lobe lobectomy

Gross description The specimen consists of a right lower lung lobe weight 470 grams with a smooth pleural surface The lung parenchyma is very soft and mushy with a salmon pink color In many areas it has a pearly white granular appearance Often the alveoli appear to be distended with this mucoid material A small portion of the most superior portion shows normal congested lung tissue The bronchi are free from tumor, and a few small pigmented hilar lymph nodes are present

Microscopical Examination The alveoli show varying degree of metaplasia and replacement by a simple columnar type of mucus secreting cell The cells are somewhat hypertrophic but well differentiated and mitoses are uncommon Varying degrees of differentiation are present and occasionally well formed goblet cells are found The cells frequently have a polypoid appearance and the alveoli are often distended by these cells The uninvolved alveoli are frequently filled with mucus and mucoid containing macrophages Occasional groups of chronic in

effusion may develop X rays show mid zone shadows of the congestive type The lung fields are infiltrated with a generalized miliary shadowing more intense in the basal zones The nodules are discrete and average 5 to 10 mm in diameter The heart shadow is enlarged Autopsy shows a typical mitral stenosis The lungs show numerous large and small infarcts some are suppurative The pleurae are studded with miliary calcified plaques On microscopic examination throughout the lung substance there are numerous rounded nodules of bone with irregular crenated outlines Vessels are present in the bone but no medullary cavities are seen A striking feature is that most of these nodules have no fibrous surrounding substance and under the microscope give the appearance of lying free of the lung The etiology of this condition is obscure Past rheumatic infection with advanced mitral stenosis is invariable It is suggested that the bone may arise from organization of congestive hemorrhages or from interalveolar collections of pigment bearing phagocytes

Pulmonary Arteriovenous Fistula

Also called varix cavernous hemangioma angioma or arteriovenous aneurysm pulmonary arteriovenous fistula is now known to occur as a multiple or solitary lesion in the lung or in conjunction with other manifestations of telangiectasia An excellent review of the literature with a report of two cases has recently been given by Yater, Finnegan and Giffin [359]

First recognized at autopsy arteriovenous fistula or aneurysm was described by Churton[382] in 1897, by Wilkens[384] in 1917 by de Lange and de Vries Robles[383] in 19 3 and by Reading[385] and Rhodes[386] in 1938 A good clinical description of the disease was first given by Smith and Horton[387] in 1939 The report of the two cases by Yater Finnegan and Giffin brings the total so far reported in the literature to 45 but almost every chest or thoracic surgery clinic has a few cases in its series At the University of California Hospital Thoracic Surgery Clinic two cases have been successfully operated upon although one has developed a fresh varix in the affected side and will require further surgery As with other pulmonary tumors a number of varixes have been discovered by mass radiography of the chest and may be removed with relative safety owing to advances in surgical technique

The condition is sometimes congenital often familial but not related

Sjogren's Disease

Sjogren's disease is a syndrome that consists of kerato conjunctivitis sicca xerostomia rhinitis sicca pharyngitis sicca and laryngitis sicca The eye lesions need not be the presenting condition Patients may first seek medical advice because of enlargement of the salivary glands Chronic inflammatory changes in the parotoid glands usually without suppuration but with recurrent exacerbations, tend to produce permanent enlargement Similar changes occur in the oral mucosa and in the lachrymal glands The glands of the skin the sweat glands, and the stomach glands may be involved The patients are usually middle aged women Associated complaints may be increased blood sedimentation rate and alterations in the blood count and in the body temperature The blood sugar curve is altered and not infrequently arthritic symptoms are present The ocular symptoms are caused by the diminution of the lacrimal secretions which results in a chronic edema gradually leading to degeneration and atrophy of the epithelium Besides the ocular changes there are secondary changes including as mentioned the mucous membranes of the nose throat pharynx and larynx Secondary dysphagia and a secondary cough may result There may be atrophic changes in the vagina also Ellman and Weber[390] report an unusual case of dryness of the bronchial mucosa with some radiological basal pulmonary shadowing of uncertain nature which may be interpreted as an infected atelectasis due to breakdown of the natural defense by the dry bronchial mucosa

Treatment X ray may be useful in the treatment in the glandular part of the disease Steam inhalation therapy may be of some use

Disseminated Ossification of the Lungs

There are two known forms of this disease trabecular which is found in the interstitial tissue of older people and nodular circumscribed which has been observed in younger people suffering from mitral disease Presenting symptoms may be increasing exertional dyspnea occasional ankle edema and a cough productive of a grayish sputum that may later become bloody Physical examination shows signs and symptoms of typical mitral disease The lungs are likely to show signs of consolidation at the bases A pleural rub may be present The temperature is usually elevated and the liver is palpable A pleural

normal hilus vascular shadow Body section radiography may establish this connection without doubt and make the diagnosis reasonably certain This failing angiocardiograms may be pathognomonic

Fluoroscopic examination is usually most helpful Pulsation may be observed in the mass Deep inspiration followed by forcible expiration against the closed glottis (Valsalva) may decrease the size of the shadow while deep expiration followed by forcible inspiration against the closed glottis (Mueller) may increase it

Differential Diagnosis Hemoptysis has led to the diagnosis of pulmonary tuberculosis A negative tuberculin test will rule out tuberculosis at once In the presence of a positive tuberculin test inability to demonstrate tubercle bacilli in the sputum or gastric contents should awaken suspicion that the disease is not tuberculosis

In cases discovered by routine x ray surveys the diagnosis of bronchogenic carcinoma has been made In this condition the diagnosis can usually be established by bronchoscopy or by the discovery of tumor cells in the sputum Polycythemia rubra vera appears in an older age group but lacks roentgen evidence except in the presence of a pulmonary infarct Immature leukocytes and basophilia are present in polycythemia vera and the spleen is more commonly enlarged

Treatment Either total or subtotal lobectomy is the only means of cure Occasionally the subsequent appearance of unrecognized lesions may require re operation as has occurred in the case at the Thoracic Surgery Clinic of the University of California Hospital The operation is now relatively safe only 2 cases of 28 having died postoperatively In small relatively asymptomatic lesions however operation may be deferred although such patients should be closely followed by periodic observation

Pulmonary Manifestations of Periarteritis Nodosa

Periarteritis nodosa is a widespread inflammatory vascular disease involving the small arteries and arterioles While the kidneys heart and liver are probably involved more frequently than the lungs the occasional occurrence of cases presenting predominant pulmonary findings either symptomatic or because of abnormal roentgen findings justifies mention of this condition among diseases of the lungs particularly since differential diagnosis is at times difficult

The incidence of pulmonary lesions in periarteritis nodosa is probably

to malignant hemangiomas, in which metastases are common Moyer and Ackerman[384] have discussed the hereditary features in a report of two cases in members of the same family

Pathology In general pulmonary fistulas have the characteristics of hereditary hemorrhagic telangiectasia (Rendu Osler-Weber's disease) The afferent artery is distended and thin walled, leading directly into one or more loculated sacs which may become enormously dilated The efferent veins are also dilated and thin walled The lesions may be single or multiple the latter occurring in over half the reported cases Rupture is not uncommon and leads to extravasation of blood into the surrounding pulmonary parenchyma and to hemoptysis

The presence of pulmonary arteriovenous fistula leads to circulatory impairment that is directly related to the size of the fistula and depends upon the unoxygenated blood passing through it The size of the shunt therefore determines the degree of anoxemia which in turn leads to symptoms of greater or lesser intensity In the cases so far reported males have predominated The condition may be recognized at birth or in adult life

Symptoms In the series of 45 cases analyzed by Yater and associates cyanosis dyspnea bleeding and weakness were the most common symptoms Epistaxis was slightly more common than hemoptysis Chest pain, dizziness, and attacks of syncope were only slightly less common The symptoms of cerebral accidents were not rare

Physical Signs Clubbing of the fingers was noticed in 31 of the 45 cases In 11 no comment regarding this condition was made A bruit was present in 26 cases Red blood cells were greater than 5 000 000 in 28 The highest count was 11,450 000 Hemoglobin was greater than 100 per cent in 25 The greatest amount was 24 9 gm Hematocrit readings greater than 50 mm occurred in 10 cases

The bruit heard over the lesion may be diagnostic It is usually continuous but may be accentuated during systole Deep inspiration may also accentuate it The heart is usually not enlarged, the cardiac output remains normal as does the blood pressure The electrocardiogram is usually unchanged but may show slight right or left axis deviation The venous pressure and circulation times are said not to be altered The vital capacity however is usually below normal

Roentgenogram The single film is not usually pathognomonic, but it may be suggestive One or more irregular areas of increased density usually in a lower lobe may appear to have some connection with the

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Roentgenogram. The single film is not usually pathognomonic but it may be suggestive. One or more irregular areas of increased density usually in a lower lobe may appear to have some connection with the

Diagnosis The occurrence of pulmonary periarteritis nodosa in patients with long standing obscure pulmonary symptoms is a possibility that should always be kept in mind Since the etiology is unknown confirmation of the diagnosis usually rests upon the finding of characteristic evidence of the disease elsewhere in the body A history of asthma with marked eosinophilia and numbness of the extremities in conjunction with the symptomology previously described is highly suggestive of the disease whether or not there are abnormal roentgen findings

Treatment Since the etiology is unknown the treatment is largely supportive consisting of bed rest for those who are debilitated a well balanced liberal diet with high vitamin content and the use of antibiotics to combat infection In those cases with bronchiectasis adequate and frequent postural drainage should not be neglected This is best accomplished by having the patient kneel on an ordinary kitchen chair hands on the floor with elbows slightly bent until complete inversion is obtained Drainage may be repeated every two hours in the beginning Later the periods may be extended

The possibility of an allergic background has been suggested by Rich[303, 304] It is probably wise therefore to withhold drugs to which the patient may be sensitive and in no case to use the sulfonamides

PULMONARY SARCOIDOSIS

The relationship between the multitudinous and widely dissimilar clinical entities that are produced when the hard tubercle of sarcoidosis invades various tissues of the body was first recognized by Schaumann[306] in 1914 He pointed out that the lungs tonsils and bones might be involved in this generalized disease which he called lymphogranuloma benigna Kuznitsky and Bittorf in 1915 described the pulmonary lesions in detail

In more recent years owing to the widespread use of the chest x ray pulmonary or hilar disease has been recognized to exist in a very high percentage of the cases of sarcoidosis Mass x ray surveys of the healthy population have brought to light many cases of entirely asymptomatic pulmonary sarcoid unaccompanied by any other evidence of the disease

Racial Incidence In most series of cases in this country Negroes have predominated out of proportion to their number in the population

more common than has been supposed Sweeney and Baggenstoss[390] found characteristic lesions of the vessels of the bronchi and lungs in 8 (28 per cent) of 28 cases observed at the Mayo Clinic Harris, Lynch, and O Hare[391] found an incidence of 29 per cent of pulmonary lesions

Pathology The pathological changes found in the arteries and arterioles of the lungs and bronchi are similar to those found in other organs Both the pulmonary and bronchial arteries are involved Early lesions present edema necrosis fibrinoid degeneration of the collagen, deposition of fibrin and cellular infiltration with neutrophiles and lymphocytes Older lesions are characterized by chronic inflammatory processes in the vessel walls which lead to distortion and scarring of the blood vessels with at times, occlusion or recanalization The process may be circumscribed involving only a minute area of the vessel, or more extensive, involving its entire circumference At times the process may extend into the surrounding pulmonary parenchyma, it is more likely to do so in lesions involving smaller vessels Granulomas consisting of lymphocytes plasma cells macrophages, and fibroblasts are usually numerous Both eosinophilic infiltration and giant cells are common

Parenchymal lesions are found in association with the vascular changes as well as independently They are early characterized by edema and necrosis with frequent hemorrhage Later, granulomatous changes occur similar to those already described with eosinophilic leukocytes and giant cells of the Langhan s type

When necropsy thickens the interlobar septa, fibroblastic prolifera tion and giant cells may be found without roentgen changes during life On the other hand it is common to find thickening of the interlobar septa on roentgen examination More extensive lesions may produce areas of increased density involving one or both lungs When these areas involve the apices they may be mistaken for the shadows of pul monary tuberculosis In the presence of long standing pulmonary infec tion, which usually has the characteristics of bronchiectasis, the roent genograms may be characteristic of the latter disease

Symptoms Pulmonary symptoms may be prominent or entirely lacking In a series of 177 cases Logue and Mullins[39] report cough as a prominent symptom in 36 per cent, pain in the chest, on application of pressure in 17 per cent and hemoptysis in 1 per cent In the 8 pulmo nary cases reported from the Mayo Clinic 2 had chronic cough that became severe 3 developed cough during the course of the disease, hemoptysis occurred in 4 cases

the entire lung field The third type shows patchy densities of various sizes scattered through the lungs and these tend to coalesce and appear fibrotic They may be confined to the mid and lower portion of the lungs or may be diffuse In addition to these general types Reisner found a few cases that often appeared unilateral and apical and identical with ordinary fibrotic tuberculosis Twenty seven cases were followed for a long enough period to report on the evolution of the lesion and about half of these regressed partially or entirely over a period of a few months to several years The majority of these lesions were the disseminated nodular type Even the large coalescent densities however may disappear entirely

Diagnosis The only entirely accurate method of diagnosis is by biopsy of a peripheral node or of a skin lesion In about 90 per cent of cases the nodes are enlarged at some time in the course of the disease and are firm rubbery discrete and non tender Often a very small node that is scarcely palpable will yield the diagnosis Daniels[8 8] reports exploration of the mesial end of the right supraclavicular fossa to obtain a non palpable supraclavicular node or even an upper mediastinal node for assisting in diagnosis when other nodes are not available

The Scandinavians have written extensively on the subject of this disease and have worked for some time in trying to develop an antigen that will give a specific skin reaction The Kveim antigen a suspension of granulation tissue from a sarcoid skin lesion will produce a sarcoid nodule in the skin of a sarcoidal individual This may also be achieved by a suspension of living avirulent tubercle bacilli (BCG) or by dead tubercle bacilli which Bjornstad found to produce the same effect in some tuberculin negative normal individuals The Kveim antigen is said to be more specific but has not been used extensively in this country

Sarcoid lesions of the phalanges of the hands and occasional lesions of the feet occur in from 10 to 20 per cent of the cases When present and found by x ray they are almost pathognomonic The bone lesions are of two main types (1) the cyst like lesion which consists of sharply outlined circular or oval rarefied areas showing no bone reaction around them and (2) the diffuse lesion with multiple irregular rarefied areas that give the bone a reticulated appearance The cortex is thinned and the shaft widened by this second type of lesion

The most helpful laboratory test is the tuberculin reaction which is negative or only weakly positive in the great majority of cases This has led to a great deal of speculation on the possible relation of this

from which the cases were drawn The age of patients has been reported to range from two months to 80 years, but the disease is most often found in the 20 to 40 age group

Pathology The fundamental lesion is the same in the lungs as it is in any other tissue—a tuberculoid accumulation of large, polygonal epithelioid cells without any central necrosis The lesion occasionally contains a few giant cells and is usually surrounded by a layer of lymphocytes but it does not provide evidence of real inflammation Occurring in the perivascular lymph spaces of the interalveolar septa these lesions in time undergo varying degrees of hyalinization and fibrous degeneration Ultimately the lymphoid structures of the lung may be entirely replaced by this tissue

The clinical symptoms are usually slight Dry cough mild exertional dyspnea and mild fatigability are the most frequent, chest pain and hemoptysis are quite rare In advanced cases dyspnea is the outstanding symptom and interference with pulmonary function may become so extreme that it produces cor pulmonale When hilar nodes only are involved there are usually no symptoms Even in massively enlarged nodes bronchoscopy has shown no encroachment on the airways Fever and constitutional symptoms are apparently present only at the time of onset or of spread of the disease if they are present at all *Physical signs* are sparse and non specific or entirely absent

Roentgenogram The most striking feature of pulmonary sarcoid is the discrepancy between the paucity of subjective complaints and physical signs and the findings of the x ray film In general the x ray shows widespread parenchymal involvement that is generally bilateral but may be unilateral At some time in the course of the disease the mediastinal and paratracheal nodes are usually enlarged Reisner,[401] in his detailed study of 35 cases proved by biopsy was able to distinguish three different types of x ray change that seem to be characteristic of different phases of the disease The first type closely resembles acute miliary or chronic hematogenous tuberculosis with diffuse dissemination of tiny nodular foci throughout both lung fields These changes may be more pronounced in the middle portions of the lung fields The second type of change is of a linear or strand like character and may be diffuse or localized The root markings become prominent, and the strands often radiate out from the roots This is much the same picture as that seen in lymphangitic carcinomatosis The accentuation of the perivascular peribronchial markings gives a reticulated lace like appearance to

Etiology The etiology of the disease is entirely unknown despite careful bacteriological and animal studies of sarcoid tissues by many investigators *In rare instances isolation of tubercle bacilli has been re* ported for the most part by European investigators Pinner[403] reports this work in detail There is an increasing body of opinion which in clines to the view that the disease is a form of non caseating tuber culosis occurring in individuals who have a low sensitivity and a high immunity to the tubercle bacillus Pinner supports this view with numerous arguments the histological picture is that of tuberculosis without caseation tuberculin anergy occurs with much too high a fre quency to be coincidental and must therefore represent a positive re lationship to tuberculosis the majority of the patients who die with the disease die of tuberculosis (he is sure that this is no coincidence) and if this be true, it does not seem strange that the Negro manifestly susceptible to tuberculosis should also have a disproportionate incidence of sarcoidosis

These arguments are countered by the fact that the sarcoid lesion is a typical foreign body' reaction and can be aroused by stimuli there is also the irrefutable possibility that patients with sarcoidosis may become secondarily infected with tuberculosis—which frequently happens in tuberculosis hospitals where patients are often confined pending diag nosis Longcope and Pierson[401] studied 8 patients exhaustively and were unable to find any evidence of tubercle bacilli and later Longcope[406] reported on 31 patients studied over a long period He does not sub scribe to the theory of a tuberculous etiology

An interesting sidelight on this problem is afforded by the occurrence of the disease in siblings Robinson and Hahn[405] report one family in which 2 out of 3 siblings had sarcoidosis and a family of 10 in which definitely 3 and probably 3 more had the disease This may indicate that a constitutional factor is involved

Spontaneous Pneumothorax

This condition may occur in the presence of obvious underlying pul monary disease such as tuberculosis emphysema abscess and cancer or it may occur in individuals without antecedent history of intrapul monary disease and in whom no obvious pathological process is present at the time pneumothorax develops Such cases usually occur in early middle life and are somewhat more common in males than in females

disease to tuberculosis. Frequently the globulin fraction of the blood serum is elevated—which may indicate that there is proliferation of the reticulo-endothelial system. The serum calcium is sometimes high. A few writers have noted eosinophilia.

Prognosis. The disease is remarkable for its extreme chronicity and tendency toward regression. The hilar nodes, often greatly enlarged early in the course of the disease, usually regress entirely, those that come to autopsy showing fibrosis only. The parenchymal lesions, on the other hand, may progress until the sarcoid deposits interfere with alveolar function to the extent of producing cor pulmonale and death. Longcope[401] reported two instances in which he found at autopsy, invasion of the myocardium in patients who died of heart failure. The majority of the fatalities, however, are from caseous tuberculosis. In those who develop frank tuberculosis the tuberculin reaction, negative or weakly positive before, becomes strongly positive. Sarcoid skin lesions often disappear promptly or become transformed into ordinary skin tuberculosis.

There is some disagreement about the benignity of the disease. Pinner[403] collected autopsy reports on 43 persons from the age of 3 months to 70 years who had died as a direct result of the disease and he objects to referring to it as benign. King[399] reported a series of 37 cases that were studied for a considerable length of time; 23 of them cleared completely or almost completely, 3 more were clearing, and only 3 progressed during the period of the study. Of Reisner's[404] series about half cleared or improved, but 7 died, 6 from tuberculosis and 1 from heart failure. Spontaneous pneumothorax has been known to occur, owing to rupture of blebs formed peripherally to partially blocked bronchi, but this complication is apparently rare.

Treatment. No treatment has been found that can be shown definitely to affect the course of the disease. It is notoriously difficult to evaluate treatment in a disease that regresses spontaneously. Roentgen therapy, however, is advocated by Oppenheim and Pollack,[402] who report a series of 42 cases, of which the 24 who had symptoms were given radiation. Of these 20 were observed for a sufficient period to justify drawing conclusions, and 17 showed complete disappearance or regression of the x-ray lesion. Curtis and Grekin[397] have treated 17 patients with vitamin D_2 and dihydrotachysterol, and they believe that these substances cause regression of sarcoid lesions and that this regression may be linked in some way with phosphorus excretion.

pneumothorax when there is no pre existing pulmonary disease He does point out, however the commonly known fact that high altitude flying is contraindicated in persons in whom a pneumothorax already exists

Symptoms The onset of the disease may be insidious or abrupt depending on the size of the aperture from which the air escapes from the lung into the pleural cavity When the aperture is small the first symptom may be a very gradually increasing shortness of breath As a rule however there is pain of varying degree on the affected side often referred to the shoulder and arm When it occurs on the left side it may be severe enough to simulate acute coronary thrombosis In severe cases the pain may be felt below the diaphragm simulating an acute surgical abdomen In severe cases too there is substernal oppression accompanied by a dry distressing cough Fever is uncommon unless blood escapes into the pleural cavity at the time of the rupture In very severe cases there may be marked displacement of the mediastinal contents toward the sound side When a one way valve mechanism is established this displacement almost invariably occurs and calls for decompression

Since more than one bleb is usually present recurrences of the condition are common Perry[415] found recurrences in 44 per cent of his series Allen Dickey[408] at the University of Wisconsin with a student population of 18 000 reported 20 cases 6 without recognized mediastinal emphysema 7 with mediastinal emphysema but without recognized pneumothorax and 7 with a combination of the two conditions

Treatment Although the disease may occur with or without effort it is advisable to forbid straining of any sort for several days after the pneumothorax has occurred In mild cases lacking pressure symptoms and with the lung only partly collapsed the leak usually repairs itself in the course of a few days and re expansion occurs whether the patient is at rest or up and about The progress is to be judged by repeated fluoroscopic or roentgen examinations In the presence of marked dyspnea with mediastinal displacement when the intra pleural pressure is found to be high, it is to be assumed that a valve mechanism has developed which allows air to enter the pleural cavity but does not permit it to escape Repeated aspiration may be practiced in these cases or a blunt needle may be inserted anteriorly in the second interspace fastened in place and allowed to communicate freely with the atmosphere With the patient in a semi Fowler s position this is unlikely to traumatize the lung further After a few days the needle may be withdrawn and the intra pleural pressures checked If they do not build up again it may be

The condition is found not infrequently among college students and numerous cases have been reported among military personnel Leach[11] reported 129 episodes in 126 cases occurring in the Army Air Force Training Command

Etiology Before the classic study by Kjaergaard,[411] ideopathic spontaneous pneumothorax was assumed to be due to sub clinical tuberculosis and patients were treated for long periods of time on the assumption that they were suffering from occult tuberculosis Not infrequently the pneumothorax was continued as a therapeutic measure in the belief that healing would be more complete with such therapy Kjaergaard, however reported prolonged observation of 45 patients, in only one of whom was pulmonary tuberculosis found to be a factor In 6 fatal cases for which autopsies were reported superficial blebs were found on the surface of the pleura but there were no other abnormalities either pleural or pulmonary Careful microscopic examination proved that a valve like mechanism was present that undoubtedly permitted air to enter the bleb but interfered with its egress, causing eventual rupture

Since Kjaergaard s report numerous investigators have confirmed these findings I have observed two cases in which thoracoscopic examination in the presence of so-called ideopathic spontaneous pneumothorax revealed several small blebs along the margins and the upper lobes one of which had ruptured At the University of California Hospital recently a medical student was found to have an ordinary small bleb on routine roentgen examination a few months later he developed a spontaneous pneumothorax on the affected side The lung expanded without complication but on complete expansion the bleb was seen to persist as before on the surface of the lung

It is not possible however to demonstrate bleb formation in all cases A few cases have been reported during high altitude flying Holter[410] and Horwitz have recorded one such case advancing the theory that the sudden decrease in atmospheric pressure caused the lung to retract from the chest wall and to rupture at the point of greatest weakness in the pleura It seems more likely however that a small bleb may have existed in this case Heath[409] reported 10 cases of spontaneous ideopathic pneumothorax in 28 000 admissions to the AAF Regional Hospital Only one of these cases occurred under conditions of high altitude flying In view of this, Heath believes that the usual conditions encountered in flight do not lead to the occurrence of spontaneous

In general diseases that may produce this type of roentgenogram and this clinical picture are non caseating tuberculosis bacterial viral and mycotic infections or diseases such as silicosis asbestosis or beryllosis which produce varying degrees of pulmonary fibrosis The lymphogenous extension of malignant tumors usually from a stomach or breast is occasionally confused with this picture Aplastic anemia and leukemia Hodgkin s disease scleroderma lupus erythematosus sarcoidosis and amyloidosis may produce bilateral pulmonary fibrosis and are sometimes differentiated with great difficulty In the presence of these confusing conditions pulmonary fibrosis of unknown etiology is useful as a temporary working diagnosis but should be discarded as soon as possible in favor of an accurate and more specific diagnosis

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assumed that the pleural wound has healed If the patient can be hospitalized he is best treated by the insertion of a mushroom catheter and the application of gentle suction under a negative pressure of not more than 10 to 20 cm of water until the lung has been expanded for several days Meanwhile penicillin should be given to combat intra pleural infection In the presence of large recurrent pneumothoraces an open thoracotomy may be indicated for the purpose of excising the bleb In stubborn cases the aspiration of air and the replacement of 50 cc of the patient s own blood has been recommended for the purpose of producing adhesions between the chest wall and the pleura

Pulmonary Fibrosis of Unknown Etiology

In spite of the most exhaustive investigation the clinician can perform he is occasionally confronted with patients who present bilateral diffuse parenchymal infiltrations or fibroses the cause of which cannot be discovered Clinically such patients complain chiefly of cough and shortness of breath which insidiously and inexorably progress Physical examination reveals only bilateral basal *rales*, and the roentgenogram shows only increased linear markings toward the bases with stippling or linear fibrosis that is not diagnostic largely because the etiological picture cannot be certainly determined Peabody Moersch and Edwards[415] have used the term pulmonary fibrosis of indeterminate origin to designate the condition

Needless to say the more detailed the study of such cases and the longer they are followed the fewer cases there will be since the etiological factor will usually become manifest during the course of the illness or at autopsy Peabody Moersch and Edwards in an analysis of 647 patients seen at the Mayo Clinic during the prior 1920 49 were able to obtain autopsy statistics on 15 cases Among these there were 2 of organized pneumonia 3 of lymphatic metastatic carcinoma, 1 each of the stomach pancreas and colon 1 of aplastic anemia produced by multiple foci of lymphocytes within the lungs, 4 cases of bronchiectasis, 1 of mitral stenosis with pulmonary fibrosis 1 of multiple pulmonary infarction 1 with widespread focal abscesses due to aspergillus infection, and 1 with pulmonary Hodgkin s disease In one case no etiological factor was found but the clinical picture was similar to that described by Hamman and Rich[414] as 'diffuse interstitial fibrosis of unknown cause'

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CHAPTER III-A

LIPID PNEUMONIA

LOUIS HAMMAN

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ETIOLOGY

In 1920 Guieysse Pellissier observed that the instillation of olive oil into the trachea of animals often was followed by an accumulation of mononuclear and polymorphonuclear cells in the alveoli of the lungs Two years later Corper and Freed published the results of a more detailed investigation upon the effects of introducing oil into the lungs Liquid petrolatum and olive oil produced proliferative bronchopneumonia chaulmoogra oil a violent acute inflammation In 1928 Pinkerton reported a still more thorough study He found that in rabbits animal oils (cod liver oil cream and lard) produce fibrosis and giant cell formation often with edema and necrosis The varying effects seem to depend upon the amount of free fatty acid in the oil or the amount liberated in the lungs by hydrolysis Vegetable oils (sesame oil poppyseed oil olive oil and chaulmoogra oil) produce little if any reaction with the notable exception of chaulmoogra oil The discrepancy in the reports of different observers concerning olive oil is thought to depend upon the varying amount of free fatty acid in different commercial preparations Mineral oil (liquid petrolatum) induces a macrophagic response with giant cell formation followed after a few months by beginning fibrosis

INCIDENCE

In 1925 Laughlen published the first observations on oil pneumonia in human beings He reported five instances four in children one in a

sprayed or instilled into the nose The oil commonly used for this purpose is liquid petrolatum *Unusual routes that have been reported are* liquid petrolatum used to anoint tracheotomy tube an oily salve allowed to trickle down the throat daily over a long period of time cream regurgitated from an esophageal diverticulum liquid petrolatum dropped into the conjunctival sac petroleum jelly used to lubricate a tracheotomy wound

The use of iodized poppyseed oil and iodized sesame oil in bronchography is for the most part without danger The oil is non irritating it is used only once and in small amount it is quickly expectorated or absorbed Apparently harm may come if exit of the oil from the lung is blocked Wright reports finding a granuloma apparently caused by the oil being trapped behind a bronchial carcinoma

From these remarks it is obvious that the chief offender in lipid pneumonia is liquid petrolatum taken by mouth as a laxative or through the nose as a spray or instillation That oil taken by mouth or used as a *spray may enter the larynx easily has been clearly demonstrated* Iodized sesame oil dropped into the nose during sleep will be discovered in the lungs the following morning Oil instilled into the nose of an animal always finds its way to the lungs Liquid petrolatum is the vehicle almost constantly used for nasal sprays and instillations because it is bland and not irritating Its use is vaunted and widely recommended to the public in advertisements The fact that it is bland is a deceptive advantage it trickles easily into the larynx and down the trachea without causing reflex cough and by coating the epithelium it hinders the effective action of cilia

Pathology —Oil after entering the lung may act (1) as an irritant causing an inflammatory reaction or (2) as a foreign body causing a macrophagic reaction followed by fibrosis To a greater or less degree all oils provoke both types of reaction the irritating oils e g cod liver oil cream lard croton oil castor oil peanut oil chaulmoogra oil chiefly cause varying degrees of inflammatory reaction the bland oils e g poppyseed oil sesame oil liquid petrolatum chiefly produce the reaction to a foreign body The changes occuring in the lungs further are diversified by the frequent introduction of infection and by the irritating effects *of medicaments added to the oils particularly to liquid petrolatum* when used as a nasal spray

To the irritating oils there is an immediate reaction more or less violent depending upon the character of the oil and the amount aspirated into the lungs The appearance may resemble that of bronchopneumonia particularly if infection has occurred and the presence of oil

man 37 years of age All had followed nasopharyngeal instillation of oil From then on reports have multiplied steadily In 1936 Ikeda collected 106 reported cases 39 of the cases being in adults In 1940 Freiman Engelberg and Merrit found in medical literature the reports of 58 cases in adults and added 47 cases from the pathological records of the Montefiore Hospital Therefore the subject is one of growing importance

Terminology

The pulmonary changes that follow the entrance of oil into the lungs have been named oil pneumonia fat pneumonia lipoid pneumonia lipoid cell pneumonia lipid pneumonia steatosis of the lungs pneumonoliposis paraffin pneumonia paraffinoma of the lungs It is desirable that future observations should be reported under a uniform designation The term lipid pneumonia seems to be the most appropriate it is coming into general use and is employed now by the Quarterly Cumulative Index Medicus

Pathogenesis and Pathology

Lipid pneumonia may occur whenever oil gets into the lungs and remains there long enough to cause irritation and set up an inflammatory reaction Introduction into the lungs occurs chiefly in two ways (1) when oil is swallowed (2) when oil is sprayed or instilled into the pharynx and nasopharynx Of the 105 cases in adults collected by Freiman Engelberg and Merrit oil had been administered by mouth in 49 through the nose in 23 both by mouth and through the nose in 5 the route not stated in 20 in the remaining 8 mainly by intratracheal instillation In this tabulation the predominance of the oral route may be explained partly by the fact that the 47 cases reported by the authors were patients in a hospital for chronic disease many of them bed ridden and debilitated others suffering from difficulties with swallowing due to disorders of the nervous system Of these 47 cases in 33 oil had been introduced through the mouth

The oral route comes into play chiefly in infants and in adults who are debilitated somnolent or in coma or else have some derangement of swallowing caused by a nervous disorder The aspiration of oil is facilitated by gagging by vomiting and by paroxysms of coughing Fish oil cream and mineral oil frequently are introduced into the lungs in this way The nasopharyngeal route is followed chiefly by medicated oils

Clinical Symptoms and Diagnosis

Up to the present time the discovery of lipid pneumonia has been an affair of the pathologists rather than of the clinicians Perhaps from now on clinicians will take a more interested and successful part in the quest Nevertheless there are difficult barriers in the way to an easy recognition In most cases the changes in the lungs come on very insidiously and cause no symptoms whatsoever In about one half of the reported cases there had been no symptoms during life to attract attention to the lungs Moreover in most of the patients with symptoms the symptoms were slight and unobtrusive not at all the kind of symptoms to warn of the presence of important pulmonary disease Most cases discovered clinically have attracted the attention of physicians by some unexpected abnormality in the physical signs or in the roentgenogram but even in these cases the correct diagnosis usually has been made at the post mortem examination Pathologists have taught us that lipid pneumonia is not an unusual disease roentgenologists are beginning to suggest the diagnosis from the appearance of the roentgenogram physicians must bestir themselves now to recognize the disease from its clinical manifestations

The most common symptom accompanying the development of lipid pneumonia is *cough* Usually it is not a severe cough and there is little expectoration The presence of fat or fat laden cells in the *sputum* should arouse suspicion Finding them does not alone make the diagnosis but it should stimulate the physician to look further If the patient is in the habit of using mineral oil the oil should be discontinued for days and the sputum then should be examined again Occasionally the sputum may be streaked with blood this probably has been due to a complicating infection

Pain seldom is complained of and rarely is conspicuous Many cases have a prolonged slight *fever* perhaps due to associated infection Others have recurring bouts of fever lasting for a few days or for weeks with the physical signs of scattered areas of consolidation many of which do not resolve

The aspiration of a large amount of oil particularly an irritating oil may be followed at once by *choking deep cyanosis* and *suffocation* Since infection nearly always is introduced simultaneously if the immediate symptoms are recovered from *septic pneumonia* may develop and later pulmonary abscess and necrosis of the lung may occur From the clinical standpoint the manifestations of lipid pneumonia may be classified as follows

in the tissues may be overlooked Abscess and necrosis may occur To the bland oils there is little inflammatory reaction though always there is some edema and cellular infiltration of the alveolar walls Phagocytes accumulate in the alveolar spaces and engulf large amounts of oil so that they come to resemble ordinary fat cells The gross examination of sections of the lungs may show scattered areas of consolidation firm sharply defined somewhat raised above the cut surface A small amount of fluid containing oil may be expressed from the nodules These areas of consolidation may coalesce and involve large portions of the lungs one or more lobes Later fibrosis advances the lesions become firmer and gray white in appearance and may resemble carcinoma Even at this stage an oily material usually may be scraped from the cut surface The character of the lesions found in the lungs will depend upon the amount of oil aspirated the frequency of aspiration the length of time the oil has been present and whether or not infection has been added to the effects of the oil

Histologically at early stages the alveolar septa are swollen and infiltrated by plasma cells lymphocytes mononuclear cells and fat laden macrophages The alveoli are filled with phagocytes containing varying amounts of fat If infection is present the exudate is more richly cellular and may contain many polymorphonuclear cells Free droplets of fat may be seen in the exudate and in the alveolar walls As fibrosis slowly develops more and more fibroblasts are found in the alveolar walls and many giant cells and epithelization of the walls of the alveolar spaces As fibrosis increases all pulmonary structure is destroyed and becomes replaced by hyalinized scar tissue usually with small pools of entrapped oil Since the most pronounced changes in the lungs are caused by the frequently repeated aspiration of small amounts of oil every stage of the process may be found side by side in a single section made from a portion of the lung The presence of fat in the cells and tissues usually is obvious in an ordinary preparation the fat globules appearing as vacuoles The fat may be stained by appropriate methods The identification of the oil that is present is determined best by extracting the oil from the tissues and subjecting it to chemical examination

In most instances the effects of the aspiration of oil are limited to the lungs and the tracheobronchial lymph nodes However, occasionally, more remote effects are observed Encapsulated masses of oil with the appearance of tubercle like lesions have been found in the spleen and liver In one case following the aspiration of cod liver oil lesions were found in the kidneys resembling those of periarteritis and glomerular nephritis

sibility of diagnosis There is no picture that is characteristic of lipid pneumonia the diagnosis depends upon the location of the lesions upon their character upon their behavior under prolonged observation and most of all upon the discrepancy between the extent of pulmonary alteration and the contrasting paucity of symptoms

As a rule the lesions are situated about the hilum and in the lower posterior parts of the lungs As one would anticipate they are chiefly in the right lower lobe and often in the right lower lobe alone In the absence of infection the shadows lack uniform density the borders are sharply defined and there is evidence of fibrosis when infection is added less circumscribed areas of consolidation occur which often coalesce with the shadows of lipid change producing a picture resembling tuberculosis These areas of pneumonia due to infection may be observed to disappear in films taken at intervals but the changes due to oil persist indeed usually grow larger and this extension of the shadows occurs in the absence of general or local symptoms Indeed the glaring contrast between the extent of pulmonary disease and the absence or paucity of symptoms is one of the most characteristic features of lipid pneumonia

Prevention and Treatment

After the reaction to oil has begun in the lung and fibrosis has developed there is no way to undo the damage In one patient a success cure has followed partial lobectomy Nevertheless much may be accomplished by recognizing the condition at an early stage and preventing further damage A little oil followed by a mild pulmonary reaction does no serious harm Only the frequent long continued introduction of oil will lead to extensive and irreparable change

The widespread use of mineral oil as a laxative needs some sensible regulation It should not be employed in infants in the aged or in those debilitated by disease or with benumbed sensorium The equally widespread use of mineral oil as the vehicle for sprays and nasal instillations is still more dangerous It is a very common practice to instill oil daily into the nostrils of infants and many adults daily spray the nose and pharynx with an oily solution Moreover these practices usually are advised by the physician since the fact that they may do harm is not generally known It will be the duty of physicians to warn their patients and the public of these dangers and to introduce some measure into the needless and unrestrained use of these remedies apparently so simple and innocent

1 In most cases the patients have no symptoms and the condition is unsuspected until revealed at autopsy

2 In another large proportion of the cases the patients have no symptoms but routine physical examination or a roentgenogram reveals *unexplained areas of consolidation in the lungs*

3 A smaller number of cases have mild vague symptoms e g cough and a slight persisting fever leading to an examination of the lungs which discloses one or more areas of consolidation usually of an extent not to have been anticipated from the mildness of the symptoms

4 Cases occur with recurring bouts of fever and evidence of areas of pulmonary consolidation resembling bronchopneumonia These symptoms are caused by recurring pulmonary infection

5 There are cases with chronic cough pain in the chest and often a little fever showing on examination massive consolidation of one or more lobes The condition may simulate carcinoma as did the interesting case reported by Thomas and Rienhoff

6 The acute cases following the aspiration of a large amount of oil are recognized easily except perhaps in the unconscious or moribund patient The clinical manifestations are those of aspiration pneumonia

7 Lipid pneumonia complicating another pulmonary disease may produce a puzzling clinical picture I recall a patient with chronic pulmonary tuberculosis of moderate extent who had large areas of consolidation and fibrosis in both lower lobes which plainly were not of tuberculous etiology and yet for the occurrence of which no satisfactory explanation could be offered Later the patient was seen by Dr Edward N Packard of Saranac Lake who made the reasonable and plausible diagnosis of lipid pneumonia although the diagnosis of this could not be verified definitely

It is almost needless to point out the great importance of the history of using oil in arriving at a diagnosis of lipid pneumonia Indeed without such a history the diagnosis would be untenable The possibility of a pulmonary disease being lipid pneumonia should be held in mind always under circumstances when the clinical manifestations are in any way unusual *The suspicion once aroused will be strengthened if the patient* habitually has used mineral oil as a laxative or as a nasal spray over a long period of time

Most cases of lipid pneumonia will attract attention first through some peculiarity of the roentgenogram the demonstration of an unexpected lesion of a lesion more extensive than the clinical symptoms had led us to anticipate or of a lesion of unusual form and distribution Roentgenologists are becoming more and more acutely alive to the pos

the entry wound over the manubrium and the exit over the acromial end of the clavicle but without any fracture of bones

Non penetrating wound limited to the abdominal wall may also produce massive collapse of the lung and it is occasionally seen as a complication of wounds of the buttocks pelvis and thighs No case of massive collapse as a sequel of a gunshot wound of the head or of the arm has fallen under the observation of the writer In the case of wounds of the buttocks and of the thighs the causation may be complex in that the injuries are often severe and frequently of such a nature as to necessitate a constrained posture of the patient often for considerable periods and so lead to restraint of the free movements of the chest Massive collapse may be fully established within twenty four hours of the infliction of the wound but the opportunities for determining the earliest period of its onset have been scanty Complete massive collapse involving one entire lung and of the contralateral type the result of a non penetrating wound of the chest wall of very slight severity has been observed fully established within fourteen to sixteen hours from the time of wounding In this instance the soldier walked four miles after being wounded It is thus clear that the essential factor in the etiology is the wound and that the condition may ensue even in its most marked form where other supposed factors such as anesthesia posture injury to the diaphragm or its nerves exudation secretion or blood in the bronchial tubes can be excluded

In rare instances massive collapse may occur in association with pneumonia thus a lobar pneumonia involving the upper lobe may be accompanied by complete collapse of the lower lobe without the presence of any gross lesion such as pleural effusion etc Massive collapse of the contralateral type is a not uncommon complication of unilateral hemothorax but it would seem to be either unknown or very rare as a complication of pleural effusion and no such case has fallen under the observation of the writer

VARIETIES OF MASSIVE COLLAPSE OF THE LUNG

In cases of traumatic origin such as those following unilateral gunshot wounds of the chest the massive collapse may be homolateral bilateral or contralateral and this applies equally whether the wound be penetrating or non penetrating The homolateral variety is often the most difficult to recognize as there must often be some doubt as to the presence or not of some gross lesion such as a small hemothorax since such a condition may be present even when the wound is a non penetrating one The contralateral variety following a unilateral non penetrating wound of the chest wall is on the whole the most striking clinical form Massive collapse may be partial lobar or total in its distribution In the partial type

peritoneum Thus the diaphragm may be affected either directly or in directly by any peritonitis present and so lead to inadequate respiration Impairment of the respiratory movements of the diaphragm may be a cause of massive collapse as is shown by the fact that massive collapse may result from the paralysis of the diaphragm seen in diphtheritic neuritis Prolonged anesthesia may induce the retention of secretions in the bron chial tubes and thus lead mechanically to the production of massive col lapse and paralysis of the diaphragm might operate in an analagous man ner Hence in considering the etiology of massive collapse the study of other varieties of the affection may be of more service Some of the most striking forms are seen as the immediate or direct result of injuries both in civil and in military practice Thus it may follow such injuries as frac ture of the pelvis or of the femur but here also the problem is complex since the severity of the injury may cause the patient to be so immobilized that the respiratory movements may be greatly hampered by the restraints imposed by posture The conditions are much more simple in the large series of cases where the massive collapse has followed gunshot wounds and it is this type of case that affords not only the simplest but also the most complete and extensive examples of massive collapse of the lung Massive collapse may occur as a result of a gunshot wound where no an esthetic has been given in the course of the treatment of the wound and where the wound has been so slight that the patient has not been confined to bed prior to the onset of the collapse Further the soldier has been in perfect health with no suggestion of previous lung disease up to the time of wounding thus such cases are peculiarly suitable for the study of the condition

Gunshot wounds of the chest are especially liable to cause massive col lapse of the lung and it is probable that it occurs in at least five to ten per cent of such injuries it is possible that the incidence is really much higher as the condition is often overlooked unless specially searched for Collapse may occur in cases of unilateral gunshot wounds of the chest either on the wounded side or on the opposite and non wounded side *i e* contralateral massive collapse or on both sides The wound causing it may be severe or trivial penetrating or non penetrating It is especially important to note that massive collapse involving the whole of one lung may occur as the result of a non penetrating wound of the chest wall without the presence of any extensive smashing of the chest wall or even without any fracture of ribs Further it may be of the contralateral type and not only is this the case but there may be no injury to the thoracic contents on the side wounded the local injury being confined absolutely to the chest wall

The wounds are not confined to those involving the lower chest wall thus extreme massive collapse has been seen after a contour wound with

opposite to that wounded since the foreign body may have been found in the wound removed and direct evidence obtained that the wound is strictly limited to the chest wall In other cases the wound has been of so trivial a character that the foreign body has dropped out on removing the patient s clothes and the wound itself has healed rapidly Physical examination reveals no lesion of the lung or exudate in the pleural cavity on the wounded side and this may be confirmed by X ray examination Striking signs however are present on the opposite side The cardiac impulse is greatly displaced towards the affected side and away therefore from the wounded side the displacement is lateral and upward the lateral displacement being usually far the greater If the left be the affected side the apex beat may be found in the axilla if the right the impulse may be felt in the right nipple line There is often marked displacement of the impulse upward and it may be palpable as high as the third rib The area of visibility of the cardiac impulse may also be increased greatly in extent The affected side of the chest is retracted and immobile and the ribs can be seen and also felt to be closer together than on the normal side The dome of the diaphragm on the affected side is also much higher than normal and the displaced diaphragm is immobile on the affected side The high level of the diaphragm can be readily demonstrated on the left side by percussion this method is not so satisfactory on the right side but X ray observation not only demonstrates the high level of the diaphragm but also reveals its immobility on the affected side The percussion note is impaired all over the affected side and dullness marked in amount may be present up to the level of the clavicle In the left axilla resonance to an abnormally high level is present owing to the altered position of the diaphragm Tactile vocal fremitus is either diminished absent or increased If diminished or absent the breath sounds are also diminished or absent if increased the breath sounds are tubular or amphoric in character In such cases bronchophony and pectoriloquy are exceedingly well marked and whispering pectoriloquy may be heard with great distinctness over a wide area Thus two groups of cases may be recognized one with diminished or absent tacticle fremitus and breath sounds and one with increased tactile fremitus together with tubular or amphoric breathing and with bronchophony and pectoriloquy In both cases extreme displacement of the heart is present The great bulk of cases conform to the type with increased tactile fremitus and tubular breathing but some cases and more especially those seen early have weak or absent tactile fremitus and breath sounds The signs however are apt to change in one and the same case thus at first weak or absent breath sounds may be present and twenty four hours later these are replaced by loud tubular or amphoric breathing with increased tactile fremitus Such changes may occur without any alteration in the degree

the upper and middle thirds of one or of both lower lobes are the parts most frequently involved In the lobar type one or both lower lobes are affected and this is the most common form but the upper lobe may be the only part of the lung involved In the variety described as total the whole of one lung is affected Massive collapse not only varies in the extent of the area of the lung involved but also in the degree of airlessness produced in all cases the physical signs suggest that no air enters the alveoli but in some cases the finer bronchial tubes would seem to be pervious while in others there is complete silence during inspiration over the area of lung involved When the area of lung involved is small there may be some increase in the size of the area while the patient is under observation but more usually the condition is fully established at the time when it is first detected Another and much more frequent variation is a change in the degree of airlessness of the lung this diminishes and the weak or absent breath sounds are replaced by loud tubular or amphoric breathing less frequently the change is in the reverse direction

Massive collapse of the lung may be the only lesion present in gunshot wounds of the chest but in a much larger number of cases it is associated with some other lesion and more especially with hemothorax In cases of unilateral hemothorax the collapse may be either homolateral or contralateral and the commonest form of the latter variety is that associated with hemothorax This association is far more frequent than the occurrence of contralateral collapse as a result of a non penetrating unilateral wound limited to the chest wall

Homolateral massive collapse associated with hemothorax is often difficult to recognize since it is obvious that the bloody effusion in the pleural cavity may itself be answerable at any rate for some of the pulmonary collapse present There is however one type of these cases that is easily to be recognized that in which a very small hemothorax of only a few ounces is associated with massive collapse involving the whole of the lung on the wounded and affected side Such cases where the collapse present is absolutely out of proportion to the pleural lesion and where pneumothorax is absent merge into others where the collapse exists without any collection of fluid in the pleural cavity

Physical Signs of Massive Collapse of the Lung

The signs are most marked and most easily recognized in cases of contralateral collapse involving the whole of one lung the result of a non penetrating wound of the chest wall limited to one side of the chest and causing no lesion to the thoracic contents on the injured side In such a case the wound is not only absolutely limited to one side but there is also no question of a foreign body having penetrated and lodged on the side

In cases of massive collapse of less extent and involving only one lobe or a portion of one lobe the signs are similar to those just described but they are necessarily more limited in area and the cardiac displacement although present is not so great as that seen in cases of collapse involving the whole of one lung The high level and immobility of the dome of the diaphragm are however always striking features of these cases

The physical signs may be summarized by saying that the pulmonary signs present a considerable resemblance to the well known signs of consolidation if anything they are rather more marked especially in the tubular or amphoric character of the breath sounds these signs are however accompanied with retraction and immobility of the chest wall together with displacement of the heart and of the dome of the diaphragm These characteristic signs sharply differentiate cases of massive collapse from other pulmonary lesions and from pleural lesions

In the other forms of massive collapse the signs are essentially similar to those described above as occurring in the cases resulting from gunshot wounds of the chest but it may be that the form most usually seen in civil practice after abdominal operations is of a somewhat different type in that inflammatory complications such as pleurisy pneumonia etc affecting the collapsed lung occur more often and hence rales and adventitious sounds are more frequently heard Similar inflammatory complications however do occur in the cases following gunshot wounds

Symptoms of Massive Collapse of the Lung

These vary greatly in severity in different cases and on the whole tend to be most marked at the onset of the condition subsiding early and even disappearing provided the patient is kept at rest in bed It is important to recognize that massive collapse may involve the whole of one lung without the presence of any urgent symptoms and the condition may be overlooked unless the chest is carefully examined and this is more especially the case in the contralateral variety of the affection If such cases are not recognized and the injured side of the chest be operated on and the pleura opened freely sudden death may occur Dyspnea is the most constant symptom in massive collapse it is usually of moderate severity but is greatly increased on exertion and even by such slight exertion as sitting up in bed In rare instances an urgent dyspnea comparable to that seen in pulmonary embolism has been described Cough usually slight but often repeated and persistent may be present together with expectoration of a muco purulent character The cough and expectoration are more marked in the postoperative civil cases than after gunshot wounds In the latter cases all expectoration may be absent throughout the duration

of displacement of the heart The alteration in the physical signs is commonly of the nature just described but sometimes a change takes place so that tubular breathing etc is replaced by weak or absent breath sounds and such alterations may occur more than once in the clinical course of the case These repeated alterations are evidently dependent upon variations in the patency of the bronchial tubes and are seen in the later stages of the condition when the chest wall is no longer immobile and some degree of re expansion of the lung is taking place They present resemblances to the well known variations in the physical signs that occur in cases of bronchiectasis

Rales and adventitious sounds may be present but they are often absent throughout the clinical course of the most marked cases even those involving the whole of one lung Adventitious sounds may however be a prominent sign in the later stages of some cases when the lung is re expanding They are also present when inflammatory complications such as bronchitis pneumonia or pleurisy develop in the collapsed lung These signs are not essential signs of massive collapse as such they are more usually to be associated either with re expansion of the lung or with the development of inflammatory complications Displacement of the cardiac impulse is certainly the most important as well as the most characteristic sign of massive collapse the condition cannot be diagnosed with certainty unless this displacement is present It is usually very considerable in amount and is always towards the collapsed lung Its duration varies sometimes it is more or less transitory and considerable changes in the position of the apex beat may occur within periods as short as twenty four or forty eight hours On the other hand it may be very persistent and three or four weeks may elapse before the heart returns to its normal position Extreme cardiac displacement may be present without the patient being aware of it or even having any cardiac symptoms When massive collapse involves either the entire lung or the upper lobe alone the cardiac displacement is upwards as well as lateral In cases of extreme cardiac displacement examination of the lung usually reveals the presence of tubular or amphoric breathing but sometimes with displacement of the heart equal to that seen in transposition of the viscera the lung signs are of the type with weak or absent breath sounds Such cases may be difficult to recognize if sufficient importance is not attached to the mere weakness of the breath sounds The heart returns towards its normal position before the signs in the lung have disappeared and it is not uncommon for the impulse to be in the normal position at a time when there is still an area of dullness with tubular breathing and pectoriloquy at the affected base Thus it is evident that an area of collapse too small to cause obvious cardiac displacement may yet give rise to well marked pulmonary signs

In cases of massive collapse of less extent and involving only one lobe or a portion of one lobe the signs are similar to those just described but they are necessarily more limited in area and the cardiac displacement although present is not so great as that seen in cases of collapse involving the whole of one lung The high level and immobility of the dome of the diaphragm are however always striking features of these cases

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of the condition and no history of an expectoration or of hemoptysis after being wounded can be obtained This is a point of some importance with regard to the causation of massive collapse The absence of symptoms is most marked in cases of collapse involving the entire lung in cases where a lobe or a portion of a lobe only is affected cough and expectoration are more frequently present Pyrexia is often absent and when present may be due to some other lesion but pyrexia is necessarily present in the cases where pneumonia pleurisy etc develop as complications of massive collapse

Duration of Massive Collapse of the Lung

The duration of massive collapse is very variable In some cases the signs clear up in a few days and the heart may return to its normal position in from one to three days after a displacement of the impulse of as much as two inches but even in these cases pulmonary signs such as a localized area of tubular breathing together with retraction of the chest wall and some limitation of respiratory movement may persist for some days The more usual course of these cases is more gradual and some three weeks may generally elapse before the return to the normal is complete The immobility of the chest disappears and the breath sounds become less tubular and are accompanied with abundant adventitious sounds such as crepitations and rales Cough and expectoration usually watery and mucoid sometimes purulent but never rusty are also present and sometimes the expectoration is not only watery but so abundant as to suggest together with the signs the presence of edema of the lung but this has not as yet been confirmed by post mortem examination the lungs examined have only shown evidence of extreme congestion

Complications in Massive Collapse of the Lung

Bronchitis especially the purulent variety pleurisy and pneumonia are the most common complications of massive collapse and definite clinical and post mortem evidence of their occurrence has been obtained It is probable that in some cases edema of the lung may occur during the stage of re expansion but absolute proof of this has not as yet been obtained

Purulent bronchitis limited absolutely to the collapsed lung has been found post mortem and this is rather remarkable seeing that in the collapse dependent upon hemothorax inflammatory complications and bronchitis are rare Although purulent bronchitis is a frequent complication of hemothorax, the lung collapsed beneath the effusion is far less affected than the rest of the lung In massive collapse the opposite may

obtain and the bronchitis be limited to the collapsed lung Pleurisy is not an uncommon late complication of massive collapse it is usually dry but effusion may occur Such cases could scarcely be recognized unless seen in an early stage when collap e only is present although when the effu ion has supervened the heart may still be displaced towards the side of the effusion owing to the extent of the collapse and the small amount of the effusion

Pneumonia of the lobar type occasionally occurs limited to the col lap ed lobe in such cases the development of the pneumonic consolidation is accompanied by a return of the heart s impulse towards its normal position

Diagnosis of Massive Collapse of the Lung

Contralateral massive collapse the result of unilateral non penetrating parietal wounds is generally not difficult to recognize Such ca es may be confused with congenital displacement of the heart or with the results of some former and forgotten chest illness The characteristic physical signs and the return to the normal after the lapse of a few days or at the most of two or three weeks afford convincing proof of the true nature of such cases When contralateral collapse occurs in association with hemo thorax on the wounded side the difficulties of diagnosis are much greater Two errors are especially likely to be made The cardiac displacement is apt to be attributed entirely to the pre ence of the hemothorax when in reality it is mainly dependent upon the contralateral collap e and secondly the lung signs tubular breathing etc are attributed in error to the supposed presence of pneumonia The high level of the diaphragm together with its immobility on the affected side affords the key to the in terpretation of these cases The following are some of the more common errors of diagnosis in cases of mas ive collapse involving either the whole of one lung or the entire lower lobe The high level of the diaphragm and the upward displacement of the heart may be attributed to the supposed existence of a subphrenic collection of gas and fluid when in reality none is present The absence of abdominal symptoms and the presence of chest signs are usually sufficient for this error to be avoided The great dis placement of the heart may be attributed to a pleural lesion on the wounded ide when none is present the wound being really limited to the pariete The cardiac displacement may be attributed to cardiac dilatation and the pulmonary signs entirely overlooked or the di placement of the heart may be thought to be of congenital origin owing to the absence of symptom The increased resonance at the left base due to the upward displacement of the diaphragm may be attributed to the supposed pre ence of pneumo thorax or to a subphrenic collection of gas Such mistakes may be

avoided by paying attention to the direction of the cardiac displacement and also to the fact that the affected side is retracted and not bulged

Massive collapse occurring by itself or on the same side of the chest as the injury is most apt to be confounded with pneumonia and this error is frequently made and can only be avoided by a thorough study of the physical signs and by specially noting the cardiac displacement For purposes of diagnosis three stages with different physical signs may be recognized In the first the signs consist of marked retraction and immobility of the affected side with great displacement of the cardiac impulse and of the dome of the diaphragm together with absent or weak breath sounds over the area of lung affected In the second stage the signs are similar with the exception that the weak breath sounds are now replaced by loud tubular or amphoric breathing with bronchophony and marked pectoriloquy The cardiac displacement may be slightly less and sometimes there is no longer complete immobility In the third stage or stage of re expansion the characteristic feature is the development of numerous adventitious sounds over the area of lung involved and now the heart is less displaced and the movement of the affected chest is more obvious

X ray examination is of the greatest possible value in the investigation of these cases and should always be employed if possible

Morbid Anatomy of Massive Collapse of the Lung

The observations on the morbid appearance of these cases are scanty The lung or portion of lung affected is obviously shrunken heavy leaden blue in color and airless Frequently it is greatly congested No obvious gross obstruction of the bronchi is present and complete massive collapse involving the whole of one lung may be present without any evidence of the existence of any gross obstruction of the main bronchus such as the presence of a blood clot or foreign body Obstruction of the bronchus by a blood clot or foreign body is of course capable of producing a condition very similar to that of extensive massive collapse but there is definite post mortem evidence that such is not the explanation of all cases of massive collapse

Causation of Massive Collapse of the Lung

The mode of production of massive collapse is obscure Theoretically it might ensue either as a result of bronchial obstruction or else as a sequel to impairment of the efficiency of the respiratory movements This in turn might result from definite respiratory paralysis as in paralysis of the diaphragm in diphtheritic neuritis or possibly from a temporary paralysis of the inspiratory mechanism of reflex origin There are difficulties in

accepting either of these views Thus there is often no clinical or post mortem evidence of bronchial obstruction and it is particularly difficult to explain the frequent absence of symptoms if the obstruction is of bronchial origin On the other hand it is not easy to understand why a comparatively trivial injury of one side of the chest should produce a reflex palsy of the respiratory muscles on the opposite side of the chest but on the whole it would seem that this explanation is the more probable

Treatment of Massive Collapse of the Lung

The condition calls for no special treatment beyond encouraging so far as the condition of the patient allows the free movement of the chest in respiration Massive collapse derives its main importance from the liability to confuse it with pneumonia cardiac disease etc and in some cases with other pulmonary or pleural lesions *e g* abscess of the lung The erroneous diagnosis may lead to the adoption of methods of treatment not only unnecessary but sometimes dangerous *e g* exploratory thoractomy

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CHAPTER V

DISEASES OF THE PLEURA

By Joseph A. Capps and Richard B. Capps

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Introduction

In a consideration of the diseases of any organ a knowledge of the special functions and physiology of the part in question obviously is essential In the case of the pleura this is especially true since in several respects the physiological and the clinical pathology are quite distinctive Thus such a characteristic as the pleural pain sense is an intrinsic part of the clinical description of pleural disease Therefore, it seems wise to open this chapter with a brief discussion of the relevant clinical pathology and physiology

Clinical Pathology and Physiology

Formation and Absorption of Fluid

As far as we know the formation and absorption of pleural effusions is dependent on essentially the same factors that govern extravascular fluids in the tissue spaces and in other serous cavities of the body The studies of Landis[1] and Drinker[2] confirming the original hypothesis of Starling[3] have shown that an increase in the intravascular venous or capillary pressure or a decrease in the blood osmotic pressure results in the production of a fluid of relatively low specific gravity Only when the capillary walls are damaged by a toxic agent or by undue physiological strain or when the lymphatic drainage is impaired is fluid of a high protein content formed In the case of the pleural cavity there is one unusual condition namely that a negative pressure usually is present A markedly negative pressure such as occurs in certain conditions[4] will increase correspondingly the tendency to fluid formation

Clinically an increased intravascular pressure is seen most commonly in cardiac decompensation and as the result of venous obstruction from intrathoracic tumors of various kinds Such fluid has a low protein content 0 5 to 1 5 per cent and is termed a transudate It should be remembered that increased venous or capillary pressure in either the pulmonary or systemic circulation theoretically can produce a transudate This is because the visceral pleura excepting the mediastinal portion is drained by branches of the pulmonary veins[5] while the mediastinal pleura is drained by the bronchial veins and the parietal pleura chiefly by the intercostals

Lowered osmotic pressure of the blood sufficient to cause a pleural transudate nearly always the result of hypoproteinemia most commonly occurs in chronic nephritis with edema nutritional deficiencies and cirrhosis of the liver It frequently complicates chronic cardiac failure

Effusions of high protein content 3 to 5 per cent or more are termed exudates They are nearly always the result of inflammation although occasionally neoplasms involving the pleura give rise for various reasons to fluids of high protein content

An increase in the negative pressure usually present in the pleural space will increase the tendency to effusion formation be it transudate or exudate Graham[4] has demonstrated this mechanism experimentally and has shown that it explains the very rapid and massive production of fluid seen in many cases of streptococcus pneumonia complicating influenza In such cases the respirations are very rapid and labored and due to pulmonary pathology the lungs lose their normal elasticity Thus the intrapleural pressure is more negative than usual

The absorption of a pleural effusion is a complicated process dependent not only on the mechanisms involved in fluid formation but also on a number of other factors as well Considerations of space limit our discussion and the reader is referred to physiological and biochemical texts for a complete discussion of the subject As in other parts of the body water electrolytes and readily diffusible substances are taken up by the blood stream whereas proteins and particulate matter are removed by lymphatics In the case of transudates fluid is reabsorbed generally when the conditions causing the formation of fluid are corrected Exudates however offer several new problems Fibrin must be liquefied before absorption is possible and the lymphatics obstructed by inflammation must become patent again When and how rapidly absorption will occur depends on the size nature and location of the exudate Large non purulent exudates and small purulent ones usually are reabsorbed However larger collections of pus seldom can be cared for by the body and either find an outlet themselves or are drained by the physician

Clinical Pathology of Pleural Effusions

The nature of pleural effusions gives important information concerning their etiology

Transudates as previously mentioned are non inflammatory and usually are clear with a low specific gravity less than 1 015 and low protein content under 3 per cent The number of cells seen under the microscope are few chiefly endothelial cells and lymphocytes Organisms practically always are absent

Exudates usually but not always are inflammatory in origin The specific gravity is high over 1 015 due to a high protein content over 3 per cent Bacteria are present if the fluid has an infectious etiology

Cellular elements usually are present in increased numbers the type indicating roughly the character of the fluid In the acute infections incited by the pneumococcus streptococcus and staphylococcus polymorphonuclears predominate In tuberculous effusions lymphocytes are characteristic although during the early stages many polynuclear cells may be present If red corpuscles are at all numerous in the fluid the evidence in favor of tuberculous infection is further strengthened

Effusions associated with tumors involving the pleura also exhibit blood often in large amount Tumor cells by special technique now being used frequently are found and identified Dock[6] considers the presence of many cells undergoing mitosis a significant finding

Eosinophiles are encountered occasionally, but their significance is not clear Frequently they are found after the absorption of a hemothorax[7] Clinical experience with cytological examinations not infrequently leaves us in doubt concerning the nature of the effusion Mixed infections contribute to this uncertainty especially when tuberculous infection is complicated by invasion with pyogenic organisms Lymphocytes can not be accepted as pathognomonic of tuberculosis since they have been found by both Miller[8] and Lord[9] when the tuberculin reaction was negative Cytodiagnosis must be looked upon as a valuable method provided it is controlled properly by other clinical evidence

A further technical diagnostic method is the analysis of air removed from a pneumothorax Frequently it is possible by such an examination to obtain important evidence in regard to the presence of a bronchopleural fistula as well as the presence of infection[10]

Intrapleural Pressure

Under normal conditions the pressure in the intrapleural space is negative due chiefly to the elasticity of the pulmonary tissue During inspiration the pressure becomes more negative and during expiration less so Changes in pressure such as occur in disease may produce profound effects This is because such changes are transmitted in varying degree to other intrathoracic structures Optimal function of the vena cava pulmonary circulation heart and lymphatics is dependent to a certain extent on a normally negative pleural and intrathoracic pressure Inequality of pressure between the two pleural spaces may also embarrass the circulation by causing a shift of the mediastinum

A pressure more negative than normal can be produced by increased respiratory activity as in anoxemia or acidosis by partial bronchial obstruction as in asthma or by obstructive atelectasis[11] As previously

mentioned such a change tends to cause the formation of pleural fluid

Intrapleural pressure becomes less negative when pulmonary ventilation is diminished as in ascites tympanites and following upper abdominal operations Emphysema produces a similar effect due to the loss of elasticity of the lungs The greatest changes are found in pneumothorax pleural effusions and intrathoracic tumor masses The effect on the circulation and the heart depends on the rapidity and degree of change in intrapleural pressure and on whether it is bilateral or unilateral Obstruction to the venous return as the blood enters the thorax probably is the greatest danger Positive pleural pressure especially if of rapid onset may result in collapse and death The presence and extent of pleural adhesions and the rigidity of the mediastinum are important factors in determining the outcome

Effusions not only diminish the intrapleural pressure by allowing the lung to collapse but also exert a hydrostatic pressure of their own proportional to the height of the fluid column Gerhardt has shown that only *in massive effusions is the pressure positive at the upper level of the* fluid

Pleural Reflexes

The intimate relationship of the pleural structures to the general circulation is understood better by considering the changes in blood pressure induced by withdrawal of fluid and by irritation of the pleural membrane

Withdrawal of fluid by a hollow *trocar or needle causes a moderate* fall in arterial pressure averaging about 20 mm Hg[1] Rapid withdrawal of a large amount increases the reaction but the effect usually is quite transitory and harmless

Irritation of the inflamed pleura has no constant influence on the blood pressure but often its effect is alarming or even dangerous Capps and Lewis[13] found that *irritation of the inflamed* visceral pleura of dogs by means of a sharp needle or chemicals in some instances caused no disturbance in others it induced considerable or even fatal fall in blood pressure A study of the latter group exhibited two types of depressor reaction 1 Cardio inhibitory with slowing of the pulse violent excursions in the tracings and slow respirations This is remedied quickly by section of the vagus or administration of atropin Even without treatment recovery is the rule 2 Vasomotor with rapid thready pulse and a steady fall in pressure that may terminate fatally

In man similar symptoms of circulatory depression or collapse occur during paracentesis and occasionally during the irrigation of the pleural cavity with antiseptic solutions notably formalin hydrogen peroxide and Dakin s solution They may appear immediately after the puncture or toward the end of the operation when the needle comes in contact with the expanding lung

Pain Sense of the Pleura

Of all the phenomena associated with pleurisy none deserves more consideration than the symptom of pain Mackenzie[14] states that the due recognition of the factors concerned in the production of pain is of the first importance in the study of disease This observation applies with particular force to pleurisy for pain is the most constant symptom and a valuable aid in diagnosis

Physiology of Pleural Pain — The nerve supply of the pleura is as follows the parietal pleura receives its innervation from the intercostal and sympathetic nerves the visceral pleura is supplied by the nerve fibers from the pulmonary plexuses which originate in the vagus and sympathetic nerves The pericardial pleura receives branches of the vagus and of the phrenic nerves The diaphragmatic pleura is penetrated on the outer side by the lower six intercostals and centrally is furnished by the phrenic nerve fibers some of which are sensory (Ramstrom[1])

Physiologists have contributed very little to our specific knowledge of the sensibility of the pleural membranes since the investigation cannot be carried on successfully in animals and these parts are not easily accessible in man Nevertheless it is to the physiological researches of Mackenzie Ross and Head that we are indebted for establishing the general laws underlying the production and distribution of visceral pain The nerves supplying the skin and skeletal muscles have become so educated that any injury to them is located accurately Such is not the case with the nerves of the internal organs A painful irritation of the viscera finds expression not necessarily over the site of the organ but in a painful area of skin often remote from it Head[16] has shown that the painful stimulus in the organ travels in a centripetal direction to the posterior part of the cord and there sets up excitation of the nerves which in the same and adjoining segments supply the peripheral surfaces with sensation The pain is referred to the skin because therein the pain sense reaches its highest development

Referred pain from the viscera has these characteristics to differentiate it from pain of peripheral origin 1 It is often remote from the site of

irritation 2 It follows lines on the skin of spinal segmentation rather than the course of peripheral nerves 3 It is associated usually with cutaneous hyperesthesia and tenderness to pressure 4 Often the pain fails to involve a whole segmental area of the skin but finds expression in one or more points of maximal tenderness and spontaneous pain

These generalizations of Head stand today unquestioned but his interpretation of thoracic pain has led him into error Rightly he states that the pain of parietal pleurisy is local following the course of the intercostal nerves But the assertions that referred pains in pleuropneumonia arise from the lungs only and that serous membranes do not give rise to referred pain are disproved by clinical experience

Lenander[17] considers the parietal pleura and pericardium to be highly sensitive to pain as well as the mediastinal tissues He calls attention to the fact that because of the overlapping of the intercostal nerve endings

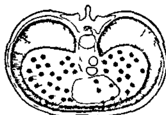


FIG 1 — Composite diagram showing the sensory supply of diaphragmatic pleura (thirty five cases) The margin in red is supplied by intercostal nerves the dotted area by the phrenic

within the thorax every point in the pleura may have fibers from at least two nerves

Experimental Production and Localization of Pain by Irritating the Pleura During Paracentesis — A simple method has been used by the senior author[18, 19] for testing the sensation of the pleura during parencentesis Through the hollow trocar a long dull pointed wire is inserted and the location of pain noted when pressure is applied to the various areas in the cavity

The observations made in thirty five cases favorable to exploration lead to the following conclusions

1 The *visceral pleura* is not endowed with pain sense

2 The *parietal pleura* is richly supplied with sensory fibers from the intercostal nerves Irritation of the pleura induces sharp pain that is located accurately by the individual over the spot that is touched Such irritation in our experience never gives rise to referred pain in the neck

or in the abdomen. The power to locate sensory impressions seems more highly developed in the anterior and lateral aspects than in the posterior.

3. The *diaphragmatic pleura* derives its sensory supply from two sources: the phrenic nerve and the last six intercostal nerves. The central portion of the diaphragmatic pleura is innervated by the phrenic nerve (Fig. 1). Irritation of this portion sets up pain in the neck. A peripheral rim of the diaphragmatic pleura, which is two or three inches wide anteriorly and laterally, and a segment corresponding to the posterior third of the membrane, are innervated by the sensory fibers of the intercostal

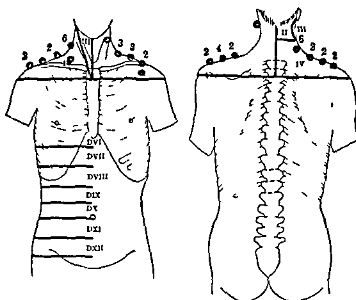


FIG. 2. — Location of maximum points of referred neck pain from diaphragm irritation in twenty-three cases. They all are situated in the regions supplied by the third and fourth spinal segments. Also there are areas of referred pain in abdominal wall.

nerves. Irritation of these areas gives rise to pain in the lower thorax, in the lumbar region or in the abdomen.

The neck pain arising from irritation of the central portion of the diaphragmatic pleura is a true referred pain, the afferent impulses reaching the cervical cord through the phrenic nerve trunk and exciting efferent impulses in the skin and superficial tissues supplied by the third and fourth spinal segments. This pain is characterized by a point of maximum pain and tenderness and by a surrounding zone of cutaneous hyperesthesia and hyperalgesia. The maximum point of pain has a remarkable tendency to appear along the ridge of the trapezius muscle, the fourth spinal segment (Fig. 2).

The pain elicited by irritation of the peripheral or posterior portion of the diaphragmatic pleura also is a true referred pain The pain usually is distributed in segmental areas over the lower thorax and epigastrium sometimes extending downward over the whole abdomen on the same side the seventh to twelfth dorsal segments (Fig 2) The pain is spontaneous and is associated with hyperesthesia and hyperalgesia of the skin and superficial tissues on pressure

The distribution of the pain is determined by the degree of irritation and by the part that is touched The more intense the irritation of the pleura the greater the tendency of the pain to spread down over the lower abdomen Rarely from strong pressure the pain is bilateral ex

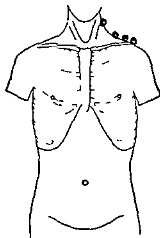


Fig 3 — Location of points of maximum pain from irritation of pericardial pleura in fourth and fifth intercostal spaces All lie in fourth spinal segment

tending over both sides of the abdomen When the posterior portion of the diaphragmatic pleura is irritated the pain is most marked in the lumbar region

4 The *pericardial pleura* receives its sensory innervation chiefly if not exclusively from the phrenic nerve (Fig 3) Only that portion which is below the fourth intercostal space however is sensitive to pain Irritation of this part of the pericardial pleura is followed by pain in the neck of the same character and in the same locations as that induced by irritation of the central portion of the diaphragmatic pleura This pain is a referred pain characterized by a maximum point of tenderness and pain by hyperesthesia and hyperalgesia to pressure of the surrounding skin and by muscular rigidity

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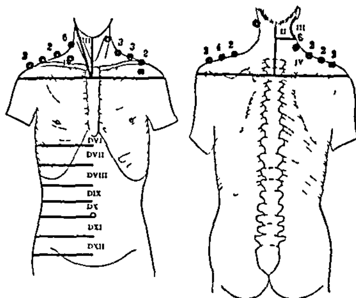


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bacillus Tubercle bacilli have been demonstrated in from 25 to 85 per cent of serous effusions according to Lord[9] either directly or by inoculation experiments

Fibrinous exudates occurring with acute pulmonary infections more often are due to pneumococcus or streptococcus Most of the empyemas complicating the pneumonias during the 1919 influenza epidemic yielded cultures of streptococcus a smaller proportion showed pneumococcus a few staphylococcus

Other organisms occasionally recovered from pleural exudates are *Friedlander s bacillus influenza bacillus diphtheria bacillus typhoid* bacillus and certain fungi It is interesting to note that pleurisy is relatively rare in three diseases in which pulmonary complications often are present influenza measles and typhoid fever The leukopenia characteristic of these infections may offer an explanation of this fact Mixed infections of pyogenic organisms with tubercle bacilli are common and often when cocci only can be found in the exudate a primary tuberculous inflammation may be diagnosed correctly by the general physical findings

Morbid Anatomy

The inflamed pleura at first is congested and acquires a dull lusterless appearance Soon an exudate of fibrin of varying thickness forms and this gives rise to the friction sounds heard over the chest during the respiratory movements At this stage absorption and organization may take place leaving adhesions or scar tissue that are permanent In the majority of instances the fibrinous exudate is followed by a serous effusion at first clear and later often cloudy from the presence of leucocytes and red cells The usual course of serous effusion is a slow absorption and recovery but if the outpouring of pus cells is excessive and continuous the fluid becomes purulent and empyema develops Nature s attempts at absorbing pus usually are unsuccessful without surgical intervention

Clinical Types of Pleurisy

The clinical course of pleurisy may end after the fibrinous stage or it may go on to the stage of effusion or it may terminate in the formation of pus For descriptive and diagnostic purposes four types are recognized (1) dry or fibrinous pleurisy (2) pleurisy with effusion (3) empyema (4) atypical forms of pleurisy

Pleurisy

Pleurisy or pleuritis is an inflammation of the pleural membranes that may involve their visceral parietal or diaphragmatic coverings

Etiology

The term *primary* pleurisy is employed when the inflammatory signs are confined to the pleura The simplest form follows exposure to cold In all probability the majority of these pleurisies are not truly primary but represent the localized flaring up of an old inflammatory process in the neighboring tissue of lung or glands Roentgenograms frequently reveal the presence of old tuberculous areas near by where the ordinary methods of diagnosis present only the evidence of the pleural involvement The tuberculous pleurisy is perhaps always secondary to an older focus of infection

Secondary pleurisy has its origin from (1) extension of inflammation from the lungs especially in pneumonia tuberculosis pulmonary abscess and infarcts (2) extension of inflammation from adjacent organs and structures notably in pericarditis mediastinitis bronchial lymphadenitis and following perforation or penetration of the diaphragm from liver abscess subdiaphragmatic abscess or cancer of the stomach (3) metastatic infection from tonsillitis in any general septicemia and in acute rheumatic fever (4) association with chronic diseases such as nephritis leukemia and gout

The lung enveloped as it is by the visceral pleura is responsible for the greatest number of pleurisies Nearly every form of inflammation of the lung involves the pleura sooner or later whether it be pneumonia, tuberculosis abscess or infarct Frequently the pleuritis is obscured by the over shadowing signs of pulmonary inflammation though the presence of pain always is indicative of pleural involvement

Bacteriology

The exact determination of the bacteria responsible for pleurisy is not always possible The sputum and the pleural exudate offer the best material for examination However in both media secondary invaders may dominate over the original organisms The bacteria commonly found are the tubercle bacillus pneumococcus and streptococcus

The frequency of old adhesions found at necropsy in the vicinity of tuberculous lesion of the lung attests the important role of the tubercle

Physical Signs of Dry or Fibrinous Pleurisy

The patient usually lies on the affected side or in a position that retards the respiratory movements on that side and breathes as far as possible with the opposite lung The respirations are shallow and rapid a protective mechanism Sudden movements of the body are painful The expansion of the diseased side is much restricted Litten s diaphragm shadow which is best observed by placing the foot of the bed toward the window and standing at an angle of 45 degrees from the feet makes a limited excursion during inspiration or is absent altogether Dyspnea is evident when pain is excessive but there is no cyanosis unless the pleurisy is a part of a pneumonic process

Exceptionally a pleuritic rub may be felt The new leather friction gives a sensation of grating to the palpating hand Tenderness to pressure in the inflamed area is common Percussion yields little information of value in dry pleurisy

A friction rub heard during inspiration and at times during expiration affords conclusive evidence The sounds are loudest over the lower part of the chest where movement is greatest and are least audible or absent over the apex where mobility is slight In the ordinary parietal pleurisy the friction generally is heard over the region in which pain is complained of by the patient As already pointed out sensation in the parietal pleura is quite sharply localized to the part irritated especially in the lateral and anterior areas Hence the painful region should be examined most carefully and repeatedly for the characteristic crepitation The rub rarely is elicited in diaphragmatic and mediastinal pleurisy until the inflammation spreads to the chest wall

The tuberculous pleurisies often apical frequently come on insidiously and may be not suspected until revealed by the stethoscope The history of intercostal neuralgia occurring periodically in the same location may be the only indication of chronic adhesions Neuralgia associated with a daily rise in temperature always should arouse suspicion of tuberculosis The leucocytes are increased more often in fibrinous than in serofibrinous pleurisy Lord s statistics showed a leucocytosis of over 12 000 in nearly forty per cent of his cases

The diagnosis of an acute parietal pleurisy ordinarily can be made from the history and auscultation Students are likely to mistake the vibratory sonorous râles of bronchitis or asthma for a pleuritic rub There is also a muscular creaking sound audible over the scapular region that is confused with a true friction This sound at times can be produced by passive movements of the shoulder blade during a cessation of

Dry or Fibrinous Pleurisy

Etiology

Dry or fibrinous pleurisy is an inflammation of the pleura associated with an exudate of fibrin The most common causes of fibrinous pleurisy in the order of their frequency are the tubercle bacillus pneumococcus and streptococcus A thick fibrinous exudate almost constantly accompanies acute lobar pneumonia The fibrinous layer found with streptococcus bronchopneumonia and abscess may be either thin or massive

Recent work has shown that fibrinous pleurisy probably is quite common in acute rheumatic fever[20, 1] The pleura is involved in this disease in the same way as are the synovia and other endothelial membranes From time to time epidemics of acute dry pleurisy have been described under various names such as pleurodynia Devil s grippe etc The etiology is unknown A full discussion will be found in another chapter (see Vol IV Chapt XXVII-A)

Symptoms

The onset may be announced by a chill and fever particularly when the pleurisy is associated with pneumonia In the tuberculous cases a chill is less common and the fever not so pronounced Many tuberculous pleurisies give a vague history of loss of weight slight fever malaise and indigestion symptoms that should lead to a careful examination of the chest Pain usually is the first and chief complaint of the patient It has a predilection for the axillary and lower anterior regions Its severity varies from a dull ache to a sharp stabbing sensation depending on the degree of movement of the pleural surfaces Because of the relative immobility of the upper lobe an apical pleurisy rarely gives rise to severe pain but more often to a soreness like rheumatism On the other hand the pain of pleurisy of the middle and lower lobes which make a wide excursion with respiration often is excruciating in character For the same reason diaphragmatic pleurisy is exceedingly painful

The pain is aggravated by cough or deep inspiration Often short unproductive cough is present provoked by the irritation of the vagus nerve endings in the pleura The pulse is accelerated and in severe cases other symptoms of general infection may appear such as headache muscular soreness anorexia and fever

Under favorable conditions the temperature and subjective symptoms subside in a few days although for an indefinite period thereafter a stitch in the side may be induced by cough or violent movement of the chest

blood and pus The factors determining the proportion of these elements are unknown or only partially understood For lack of specific information we assume that the quality and virulence of the infecting organism on the one hand and the individual reaction of the tissues on the other hand are chiefly concerned However the type of inflammation that will be excited by an organism cannot be predicted Thus the tubercle bacillus may cause a simple fibrinous serous hemorrhagic or purulent exudate A pneumococcus pleurisy may terminate in the fibrinous serofibrinous or purulent stage The same variety of exudates prevails in pleurisies accompanying pneumonia and cancer

The serous or serofibrinous effusion with an amount of fluid sufficient to give physical signs generally is of tuberculous origin Norris and Landis[99] quote figures that bear this out It is estimated that between 70 and 80 per cent of all cases are tuberculous Only rarely can the tubercle bacillus be recovered on a cover glass preparation or in the cultures but inoculation of guinea pigs with the fluid causes death from tuberculosis in a high percentage of cases Frequently too an effusion occurs in association with tuberculous lesions in the lungs and bronchial glands Serous exudates of pneumococcus origin are less common than the fibrinous They have a greater tendency to become purulent than the tuberculous form and usually are more localized Occasionally streptococcus effusions remain serous but all the pyogenic cocci show a disposition to pus formation Acute rheumatic fever is of all general infections most often complicated with serous pleurisy[90 1] In this condition the pleural membranes are affected directly in a manner similar to that of the synovial membranes As a terminal condition in cancer heart disease and nephritis serous effusion frequently develops and may be confused with a transudate

Symptoms

A patient may consult his physician complaining of shortness of breath rheumatic pains in the chest fatigue and loss of strength Examination reveals a large accumulation of fluid in the chest Such is the history of many cases of the tuberculous type Rarely one sees the acute fulminating type the pleurisy acutissima which is characterized by a progressive accumulation of fluid Dyspnea and cyanosis may be present but not always to an alarming degree Without warning the patient may become pulseless and die Such a termination is avoidable by early aspiration of the fluid Another group follows in the wake of pneumonia and provokes no other subjective symptom than increasing

respiration and usually is bilateral The unusual types of pleurisy will be discussed later

Prognosis

The prognosis of a simple dry pleurisy is good so far as the immediate infection is concerned A considerable proportion in later years will develop signs of pulmonary tuberculosis The outlook in metapneumonic cases is determined by the course of the lung lesion Diaphragmatic pleurisy adds to the gravity of this group only as it intensifies two unfavorable factors in pneumonia pain and dyspnea

Treatment of Dry or Fibrinous Pleurisy

Rest in bed should be enforced regardless of the mildness of the symptoms Complete rest may have a profound influence on the course of the disease Pain is the one symptom demanding relief Nothing is as effective as codein or morphin to control the early pains and cough As the suffering becomes less severe aspirin may be used Strapping the affected side with adhesive plaster or the use of a snugly fitted swathe of light canvas gives partial relief Heat or cold locally applied are both helpful especially cold in the form of an ice bag Strips of bandage chilled on a cake of ice and repeatedly applied to the tender area have a remarkable anodyne influence The older physicians were much given to dry cupping over the seat of the pain and this procedure is well worth trial

In diaphragmatic pleurisy strapping of the chest often increases pain by exaggerating the movements of the diaphragm Pressure of a bandage about the abdomen is at times grateful to these patients

Pleurisy with Effusion

Pleurisy with effusion is an inflammation of the pleura associated with exudate that may be serous serofibrinous seropurulent or hemorrhagic

Etiology

It is well to keep in mind that all the clinical types of pleurisy are classified arbitrarily A dry pleurisy more often than not will yield a few drops of serum to the exploring trocar The terms employed are derived from the predominating elements found in the exudate fibrin serum

The diseased side is less mobile than the healthy one as shown by the limited motion of the shoulder The interspaces are less concave than normally and under great pressures may bulge Litten s diaphragm shadow is absent unless the fluid is small in amount or encapsulated in the upper portion of the cavity One sees the apex impulse either to the left of the left nipple or to the right of the sternum according to the side of the chest involved In many instances where the effusion is large or the adipose layer is thick the cardiac impulse is not visible especially is this true of left sided pleurisies

By placing the hands on both sides of the chest during deep respiration a difference in expansion may be observed Also the cardiac impulse can be better located by touch than by sight The most valuable sign elicited by palpation is pectoral fremitus Three distinct zones can be differentiated under favorable conditions in an effusion of moderate size The lowest zone transmits either a weak vibration from the spoken voice or none at all The zone just above the fluid level gives an abnormally strong tactile fremitus owing to the heightened transmissibility of the sound waves through the layer of relaxed or atelectatic lung Over the upper zone the fremitus is normal A thick fibrinous exudate also impairs the pectoral fremitus so that the sign cannot be depended upon

The value of percussion depends on careful skillful technique as well as on proper interpretation of findings At the beginning of the examination the sound side should first be gone over and the borders of the heart and liver determined Loud forcible percussion often is required in fleshy or dropsical subjects but a light stroke is preferable in outlining the fluid level and is almost essential in small or circumscribed exudates It is more convenient and satisfactory to have the patient in a sitting posture when the patient is not too ill safely to sit up

Dullness or flatness is the distinctive note over the effusion but a considerable quantity of fluid up to 500 c c may be present without creating a noticeable change in the sound Above the fluid the note frequently is hyperresonant or tympanitic the so called Skoda s resonance The upper border of fluid follows a curved line the S curve of Ellis which ascends from the anterior wall to the highest point in the posterior axillary space then descends to its lowest level at the spine The triangular space of Garland overlies the lung retracted toward the spine and is characterized by a hyperresonant note When the effusion is large flatness extends over this space and over the upper portion of the chest The region last to lose its resonance in massive exudates is the subclavicular space which often remains tympanitic

Effusion on the left side may fill Traube s semilunar space giving rise

dyspnea The temperature may remain elevated after the crisis and the pulse be accelerated

Fever of moderate degree is common but in no sense typical As a rule the temperature rises during the secretion of fluid and becomes irregular or normal during absorption More depends on associated or underlying conditions in influencing the temperature than the pleurisy itself The course of a lung abscess a tuberculous infiltration an arthritis or a septicemia is likely to dominate the temperature curve In the aged and in terminal pleurisies the temperature may remain subnormal throughout

The acute pain so characteristic of the dry pleurisy disappears as the effusion separates the membranes and gives place to diffuse muscular pains Cough is not incited by an effusion per se When cough is present one looks for its source in a bronchitis The sputum is surprisingly scant in the primary cases but in secondary cases varies with the nature of the basic disease

The respiratory rate which we have seen is accelerated by the pain in dry pleurisy becomes more normal during the accumulation of fluid and cyanosis is less conspicuous than one would expect The pulse responds to the influence of temperature and pain Hence with the progress of an exudate the pulse may be slow The arterial tension is maintained even when the exudate is large although the pulse volume may be diminished When however the fluid pressure is excessive the arterial tension falls

Sweating is as characteristic of pleurisy as it is of articular rheumatism The amount of perspiration is not dependent on the fever alone but on other factors causing a vasomotor dilatation The sweats are followed by a sense of weakness and exhaustion

The urinary output undergoes a decided diminution during the formation of the exudate and is further reduced by the sweating A rise in the daily excretion often heralds the beginning of pleural absorption Albuminuria and casts may be found in the urine but seldom is the renal complication serious Headache indigestion and general weakness are met with commonly resulting no doubt from the infection

Physical Signs of Pleurisy with Effusion

The attitude of the patient may be suggestive as he attempts to leave the sound side free and usually uppermost if he lies on the side As the effusion grows larger the upright posture often is assumed Cyanosis and dyspnea are not conspicuous in small and moderate effusions Irregularity of the pupils may be detected the pressure on the pupillary fibers of the cervical sympathetic causing a dilatation of the pupil on the affected side

picture requires experienced interpretation as do other physical signs but it has contributed greatly to accurate diagnosis

Exploratory puncture of the chest for diagnostic purposes at one time was looked upon as a last resort when other methods failed Today the *procedure is considered a legitimate part of a careful examination* The information derived from puncture is (1) the presence or absence of fluid (2) the nature of the fluid whether serous purulent or hemorrhagic (3) the bacteriological findings Perhaps the most practical value is to determine if there is pus present for if such is the case drainage usually is essential to bring about the recovery of the patient Often a puncture *reveals consolidation where fluid was suspected but no harm results even* if the lung is entered

Clinical Course of Pleurisy with Effusion

The clinical history of a serofibrinous pleurisy depends upon the nature of the exciting organism the complication of other diseases especially of the lungs the resistance of the individual and finally upon the treatment A stormy onset with chills and fever is not necessarily unfavorable for often absorption is rapid and complete An extensive friction rub usually is followed by moderate effusion Large effusions more often arise insidiously with a minimum of pain and often unaccompanied by friction sounds The tendency in a simple pleural effusion of moderate size is to gradual absorption with more or less formation of adhesions between lung and pleura

A massive effusion rapidly accumulating pleurisy acutissima is an immediate menace to life The danger cannot be measured safely by the subjective symptoms or by the pulse rate arterial tension dyspnea and cyanosis Sudden death may occur in these cases unless the fluid is withdrawn The explanation of this collapse is rarely found in a pulmonary embolus More often the necropsy fails to reveal any anatomic lesions The mos plausible theory is the one advanced by Rosenbach[21] that the increasing intrathoracic pressure reaches a point where obstruction to the vena cava takes place resulting in a failure of blood flow into the heart

The development of pulmonary tuberculosis after pleural effusion is not uncommon This sequel may be explained either on the basis of a primary tuberculous infection of the pleura or a subsequent implantation of tubercle bacilli on a favorable soil

The conversion of a primary serous effusion into pus is comparatively rare occurring only 16 times in 1 183 cases reported by Lord Serofibrinous exudates secondary to pneumonia on the other hand frequently change into empyema

to dullness or flatness instead of the normal tympany transmitted by gas in the stomach or colon The sign loses much of its worth because of the frequent presence of pleural adhesions or distention of the gastrointestinal tract with food

Another region of some importance is the paravertebral triangle (Crocco s) a dull area at the base of the sound side of the chest posteriorly the apex beginning at the upper level of the fluid and running diagonally downward to the base line This is caused by a displacement of the mediastinum the lower part yielding to a greater hydrostatic pressure than the upper part

The displacement of organs is a most striking result of pleural accumulations and is recognized more readily by means of percussion than by inspection Depression of the diaphragm may force down the liver so that its border may be found by percussion or palpation well below the costal edge The spleen on the other hand is rarely displaced far enough to palpate Displacement of the heart can be demonstrated by percussion in the absence of visible or palpable evidence Dislocation of the posterior mediastinum has been touched upon already

During the absorption of an effusion or after drainage percussion shows a gradual return of the normal resonance A favorable sign is the extension of resonance at the lower border during inspiration which indicates the expansion of the lung with air Demonstration of moveable dullness is almost pathognomonic of effusion Unfortunately it is not a constant sign It is obtained by locating the lowest interspace of resonance in the recumbent position upon assuming an erect position this space becomes dull or flat Numerous conditions interfere with the free shifting of fluid notably adhesions massive exudates and emphysema It is most often observed in recent exudates of moderate size and in hydrothorax

If one is so forturate as to examine a pleurisy at the onset he hears a pleural crepitation or a friction rub As the fluid collects and compresses the lung the vesicular respiratory sounds disappear and bronchial breathing is heard perhaps faintly and at a distance Above the fluid moist rales may be audible The voice sounds likewise become distant and altered in quality according to the depth of fluid and condition of the lung When the bronchi are clear and the retraction of lung slight bronchophony or the more nasal egophony are present In the presence of an excessive effusion the voice sounds are completely muffled Baccelli s observation that the whispered voice is transmitted through a serous effusion but not through pus has not proved a trustworthy sign

It has become almost a routine procedure in hospital practice to inspect the chest with the fluoroscope and take x ray films The Roentgen

pleural membrane is relatively normal and responds to osmotic pressure Therefore a restoration of the circulation will favor absorption of the fluid Likewise a depletion of the body fluids by means of a low liquid intake or abundant elimination will tend to establish the flow of fluids away from the pleural cavity On the other hand exudate is an inflammatory process in which the accumulation is produced by the secretory activity of the endothelial cells of the pleura The pleura itself undergoes the changes of coagulation necrosis bringing about an occlusion of lymphatic and blood spaces The pleura is no longer a membrane responding to osmotic influences The cavity is walled off temporarily Hence the measures above mentioned no longer are efficacious Inflammatory secretion may take place even in dysentery when there is general dehydration of tissues The pleural fluid may remain unchanged in quantity after purgation free diuresis and sweating

At the beginning of an exudate and at a late stage when the fibrin is undergoing digestion the pleura may have a certain degree of permeability There are also borderline effusions between transudates and exudates in which the pleural membrane permits the exchange of fluids Our therapeutic efforts may be followed then by positive results but we cannot expect success in a majority of cases

Restriction of liquids should not be enforced below a liter daily The patient needs a diet of 2 500 calories to overcome the great weakness The skimmed milk diet of Karell is not adequate to maintain the patient s strength Hydragogue cathartics are of especial value at the onset Epsom salts or compound jalap powder are serviceable Excessive catharsis should not be continued however for many days Diuretics often are employed caffein and theocin giving good results Sometimes a spontaneous diuresis ushers in the period of absorption Diaphoretics are not recommended because of the excessive sweating that naturally accompanies the disease Cardiac stimulants seldom are indicated unless there is an associated myocarditis

Iodides deservedly are losing their former popularity as absorption agents in pleural exudates The known power of iodide is to bring about liquefaction and absorption of granulomatous deposits such as the round cell infiltrations of syphilis and actinomycosis In the rare instances where these infections invade the pleura the administration of iodides is rational But there is no evidence that the drug has any influence on the ordinary exudates

4 *Thoracentesis* — Drainage of pleural effusions by thoracentesis has taken its place as the most important of all therapeutic measures for this condition Practiced since ancient times by a few of the bolder spirits

Diagnosis

The recognition of a primary serous pleurisy ordinarily presents little difficulty because the physical signs are characteristic. The secondary cases need to be differentiated from pneumonia. Both effusion and consolidation give dullness and may exhibit bronchophony but in the latter the viscera are not displaced. A thickened pleura is not always easy to distinguish from pleural effusion and the two conditions may both be present. Exploratory puncture will clear up the diagnosis. Puncture is also necessary to diagnose definitely a small or circumscribed exudate. A tumor mass gives rise to flatness on percussion and its presence often is suspected for the first time after a dry tapping. Occasionally the introduction of a small amount of air 10–20 c.c. is helpful. By creating a fluid level on the x-ray film it aids in differentiating pulmonary consolidation from fluid.

Treatment of Pleurisy with Effusion

The treatment of serofibrinous pleurisy may be considered as follows:

1. *Treatment of the Infection.* — The most favorable time for influencing the course of the infection is at the very onset. Rest in bed when promptly enforced may modify entirely the severity of the disease both by securing relative quiet for the inflamed pleura and by increasing the resistance of the patient. A saline purge and a hot bath are advisable. The diet should be light. Specific remedies are lacking. Salicylates are thought to have some special action in rheumatic cases but as they do not materially alter the progress of the arthritis they cannot be expected to materially influence the pleurisy.

2. *Symptomatic Treatment.* — The symptomatic measures of relief in the early stages are the same as in fibrinous pleurisy. The pain becomes less severe as the fluid increases and cough becomes less troublesome.

3. *The Promotion of Absorption.* — Much has been written on the subject of preventing the formation of fluids and encouraging their absorption after their accumulation in the chest. The measures employed for these purposes are the limitation of liquids in the diet and excessive elimination of fluids by the organs of excretion. Clinical experience bears testimony to the fact that these measures often are successful in transudates and rarely so in exudates. There is an essential difference in the two conditions that must be kept in mind in our therapeutic procedures. A transudate is non-inflammatory in origin and is brought about as a result of venous stasis as occurs for example in cardiac decompensation. The

of breath on exertion At the present time this type of pleural effusion is more neglected than any other either because of a reluctance of the physician to operate or because of a mistaken diagnosis of pleural thickening The results of drainage always are beneficial although expansion seldom is completely restored Exploratory puncture for diagnostic purposes has been referred to previously

The Time of Preference for Operation — In a typical case of pleuritic effusion the fluid collects gradually for several days During this period the endothelial cells are in a state of inflammation that keeps up a steady secretion and it is probable that the presence of fluid separating the opposing membranes exerts a favorable influence on the inflamed surface In other words the fluid serves as a protective covering as it does in an inflamed joint Complete evacuation therefore is not advisable until the acute stage has passed always excepting those conditions of urgency just discussed The time of the quiescence of endothelial activity can be determined by the subsidence of fever and by the stationary level of the effusion As a rule this takes place in a week or so after the initial symptoms Tapping at this time of election is followed by less rapid and abundant reaccumulation of fluid whereas very early evacuation is likely to result not only in a quick return of fluid but in exacerbation of fever The fever however does not justify a long delay in tapping after the exudate has become stationary for in some instances the temperature actually falls after the drainage of the cavity

Late tapping is recommended especially in pleural effusions associated with pulmonary tuberculosis Koniger[7] has emphasized the favorable influence of the exudate on the basal disease The compression of the lung with atelectasis and the formation of fibrous adhesions are most desirable for promoting the healing of tuberculous infiltration He advises the postponement of tapping for two weeks or longer Then only a portion of the fluid should be taken away When the effusion is small or moderate in amount often it is advisable to let the fluid remain

Posture of Patient — The sitting position is rather more convenient for the operator as the patient can elevate the shoulders and spread the ribs apart but it is decidedly bad for the patient The upright position greatly exaggerates all circulatory disturbances especially inducing cerebral anemia and faintness The recumbent posture should be preferred always the patient lying on the back or side with the shoulder raised on the side affected The opinion is prevalent that evacuation is greatly favored by the upright position but as a matter of fact the rate of outflow is regulated more by the intrapleural tension and the action of the diaphragm and intercostal muscles than by hydrostatic pressure

the method was placed on a sound clinical basis by Laennec[4] and Trousseau[5] and introduced in America by Henry I Bowditch[6] and Morrill Wyman

The indications for tapping formulated by Bowditch[26] in 1852 cannot be improved upon today (a) When the chest is full in either acute or chronic cases (b) when alarming dyspnea is present even if the quantity of fluid is small (c) in all cases where absorption is slow

The acute cases with rapid accumulation of a large amount of fluid have been referred to already Trousseau became convinced of the necessity of immediate drainage in these cases to prevent death and coined the expression indicatio vitalis Most hospital clinicians can recall instances of effusion filling most of the pleural cavity where tapping has been delayed on account of the absence of marked dyspnea and cyanosis in which death occurred unexpectedly When the fluid reaches the spine of the scapula behind or the level of the third rib in front tapping should be carried out without delay Fever is no contraindication The fluid is likely to reaccumulate and require repetition of drainage If one waits for a marked fall in blood pressure it may be too late to save the patient Fortunately this acute type of pleurisy is rare

Massive effusion of gradual development is much more common than the acute cases with very rapid accumulation Occasionally a large effusion has been present for weeks or months before it is recognized The constant pressure weakens the intercostal muscles flattens out the diaphragm and destroys its function and displaces the heart Myocarditis may supervene as a result of chronic infection Under these circumstances some unusual exertion such as a paroxysm of coughing sudden change of position or thoracentesis may throw the patient into collapse Tapping is imperative in this group of cases and should be performed with as little shock as possible and only a portion of the fluid should be withdrawn at the first operation

Marked dyspnea and cyanosis are indications for thoracentesis regardless of the amount of fluid present Encysted pleural effusions in the mediastinum or near the heart may cause symptoms out of proportion to the quantity of effusion Under these conditions evacuation of a few ounces may bring considerable relief

Failure of absorption or very slow absorption in effusions of moderate size calls for mechanical interference Such an exudate is practically encysted and consequently may cause very little toxemia The long continued presence of fluid however compresses the lungs and establishes firm adhesions which prevent the ultimate restitution of function The patient usually is able to walk about and may complain only of shortness

upper border of the rib thus avoiding the artery that runs along the under surface of the rib Care hould be taken not to scrape the sensitive periosteum and thus cause unnecessary pain

When the pleural cavity is entered the stilette is withdrawn and the fluid escapes The flow usually is spontaneous slowing with inspiration and increasing with expiration Siphonage is the ideal method of evacuating fluid and should be practised wherever possible To prevent the inward suction of air a rubber tube three feet long is attached to the canula and suspended in a bottle In large effusions where the positive pressure is considerable and when the lung is expansile and the diaphragm is mobile a large quantity may be obtained by siphonage alone But in many cases the spontaneous flow ceases before the bulk of fluid is removed or even after a few ounces have escaped because of a negative intrathoracic pressure It then becomes necessary to aspirate

In all methods of aspiration the tube leading from the canula is attached to a large bottle in which a partial vacuum is produced The best apparatus is that of Potain which creates a measured degree of suction by an exhaust pump By turning a cock on the connection between the bottle and pump the negative pressure can be maintained Occasionally the novice makes the wrong connection and pumps air into the bottle instead of exhausting it and this forces air into the chest As a precaution the apparatus should be connected and tested by sucking up sterilized water with the tube that connects with the trocar canula

The rate of withdrawal should be slow In hospital practice too often by rapid evacuation the patient s welfare is sacrificed to the convenience of the interne Slow drainage favors the gradual expansion of the lungs the replacement of the dislocated heart and the ascent of the diaphragm Rapid evacuation causes engorgement of the pulmonary vessels and lowers the systemic arterial tension more than slow drainage Faintness may ensue and terminate the operation prematurely It is a good rule to use the minimum degree of suction and take plenty of time

How much fluid should be withdrawn depends on the total quantity present in the cavity and the degree of suction required to keep up the flow Not more than 1 500 c c should be taken away even under favorable conditions If the exudate remaining still is considerable it is better to resort to repeated tappings in order to reestablish the function of the compressed lung

Complications Attending or Following Thoracentesis

In the great majority of cases thoracentesis and drainage of an effusion is a simple procedure not attended by any untoward symptoms By

There are complicating conditions which render the upright position obligatory as in asthma cardiac decompensation and pericarditis

Preparation of Patient — Aseptic precautions are necessary as in all surgical procedures The skin is painted with tincture of iodin or washed with soap and water followed by alcohol Over the site chosen for puncture a saturated solution of phenol may be applied for twenty seconds and then washed off with alcohol thus effecting a degree of anesthesia in addition to antisepsis Novocain usually is used in old or nervous patients but to be satisfactory must penetrate the deep sensitive intercostal tissues as well as the parietal pleura Freezing the skin with ethyl chloride a convenient anesthetic serves to mitigate the cutaneous pain General anesthesia is contraindicated in thoracentesis because it favors pulmonary edema and respiratory failure All instruments should be sterilized and the hands of the operator thoroughly cleansed with soap and water and some antiseptic solution

Site of Tapping — The needle is inserted over the area of flatness as low as feasible As a rule the midaxillary line in the sixth or seventh space is a desirable location because the muscular wall is thin and the intercostal spaces are wide The seventh and eighth spaces near the angle of the scapula are particularly favorable to drainage of small effusions which may not extend to the front of the chest A dry tap over one area should not be discouraging for a thickened pleura may block the needle at any given spot Often a second or third puncture at different locations is rewarded by a free flow Encapsulated or interlobar effusions should be tapped where the physical signs and the x ray photograph show the easiest approach to the fluid

Technique of Thoracentesis — The choice of instrument needle or trocar is largely a matter of individual preference A hollow needle with a lateral foramen is more easily inserted and causes less pain than the trocar The needle should be at least 2 mm in diameter as one with a smaller caliber often is occluded by a thick effusion Occasionally the sharp point works an injury to the diaphragm or lung and as the lung expands may cause irritation of the visceral pleura This irritation sometimes provokes a troublesome cough and exceptionally circulatory disturbances unless the instrument is withdrawn

A medium sized trocar with a smoothly fitting stilette is a safer instrument and by many preferred to the needle for therapeutic purposes For exploratory tapping however when several punctures may be necessary the needle is the instrument of choice The finger of the left hand is pressed in the interspace selected and the upper margin of the lower rib well defined The trocar is inserted inward and slightly upward over the

upper border of the rib thus avoiding the artery that runs along the under surface of the rib Care should be taken not to scrape the sensitive periosteum and thus cause unnecessary pain

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many the operation is looked upon as of no more gravity than paracentesis of the abdomen in ascites but there is an essential difference in the two conditions In ascites the fluid is always under a positive pressure and drainage is accomplished by siphonage alone whereas in pleural effusions the intrathoracic pressure may be zero or negative and aspiration therefore is required Aspiration produces sudden and radical changes in the intrapleural tension which directly affect the pulmonary circulation the action of the heart and the respiration Most of the untoward symptoms occur toward the end of aspiration or within a few hours after the operation Many of them can be prevented or mitigated by observing certain precautions to avoid too sudden or excessive alterations in the intrathoracic pressure Too much emphasis cannot be laid on the fact that siphonage is comparatively free from these complications

Pain usually is very slight after the trocar is inserted Contact with the visceral pleura or penetration of the lung does not give rise to pain When the trocar touches the diaphragmatic pleura however and this is not a rare occurrence then pain is severe and referred to the neck or to the lower costal region Partial or complete withdrawal of the needle is indicated

Cough rarely occurs during the siphonage and during aspiration is observed most often after the withdrawal of a considerable amount of fluid It is produced by irritation of the nerve endings of the vagus probably as a result of pulmonary congestion Contact of the trocar with the pleura seldom is the exciting cause When the cough is persistent there is danger of tearing the lung and also of edema so that it is best to withdraw the instrument Morphin and atropin can be used with advantage before an evacuation

Faintness is encountered frequently when the patient is sitting upright especially in nervous individuals For this reason the recumbent position is advisable When faintness results from the pain of the puncture or from psychic disturbance a dose of whiskey or aromatic spirits of ammonia will restore the circulation without interference with drainage Another type of faintness not yielding immediately to stimulation is due to the excitation of the pleural or pulmonary nerves and occurs usually toward the end of drainage This demands instant termination of the operation The pulse is weak and frequently slow in faintness of both types As a rule faintness develops when the systolic arterial pressure approaches 60 mm of mercury but the condition generally is transitory

Hemorrhage may result from the wounding of the intercostal artery but this is a rare accident and can be remedied by applying a ligature Pulmonary hemorrhage has been reported from penetrating consolidated

lung tissue In most of these cases a tuberculous cavity is entered and an artery wounded Piercing the lung in lobar pneumonia is a common incident in exploratory puncture but in the author's experience seldom has been followed by hemorrhage Absolute rest and morphin are the best remedies if pulmonary hemorrhage occurs

Infection of the exudate converting the effusion from a serous to a purulent fluid must be a very rare incident A transformation of serum into pus may occur spontaneously in the pleurisies secondary to pneumonia Moreover empyema may be induced or hastened in certain instances by the withdrawal of serum which Opie has shown is due to chemical and not bacterial influences

Subcutaneous emphysema is an interesting complication seldom serious that occasionally arises from puncturing the lung The air escapes along the needle track to the subcutaneous tissues and may spread over the chest and even to the neck A localized edema is observed near the site of the tapping and a characteristic crackling sound can be both felt and heard The condition lasts only a few days

Pneumothorax of some degree can be demonstrated quite commonly a day or two after tapping Frequently a little air is sucked into the cavity through loose fitting connections of the apparatus A hyperresonant note over the upper level of the fluid arouses a suspicion of air as the sound is more tympanitic than the Skodaic resonance A shifting of this area and succussion sounds elicited by shaking the chest confirm the diagnosis The admission of air during thoracentesis is not at all detrimental and may even serve a useful purpose so long as it does not exceed in volume the fluid withdrawn No treatment is necessary and in a few days it is absorbed

When however the pneumothorax results from a laceration of the pleura and lung the situation is serious for the air is forced through the opening into the cavity until the wound closes

Edema of the lungs is a complication that may be fraught with grave consequences It comes on generally toward the end of the evacuation or a short period afterward Accompanying the edema is a cough with expulsion of an abundant pinkish frothy material the so called albuminous expectoration Dyspnea and a failing circulation may ensue with a fatal termination The pathology of this condition is somewhat obscure but an important etiological factor is the intense congestion of the retracted or atelectatic lung after the release of the compressing fluid There is much reason also for accepting the theory of Cohnheim namely that the vessel walls of the compressed lung have undergone degenerative changes as the result of the compression affecting their nutrition Possibly in some cases nervous reflexes may be a factor as described by Hes [73]

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The clinical conditions which induce pulmonary edema are the too rapid evacuation of fluid the drainage of an excessive quantity and the employment of too much negative pressure during aspiration The avoidance of these measures will go far to prevent the development of edema There are nevertheless some instances of edema subsequent to drainage of a small effusion even when siphonage alone is used

The appearance of frothy expectoration is a signal for instant cessation of drainage On theoretical grounds the introduction of a few hundred c c of air to replace a portion of the fluid removed should prove beneficial Morphin and atropin have been the most successful of the many remedies employed for relief Adrenalin is contraindicated because in experimental work often it has produced pulmonary edema

Collapse and Sudden Death from Thoracentesis and Irrigation of the Pleural Cavity — Sudden circulatory failure has been described in connection with edema and with the laceration of a pulmonary artery But there are cases of sudden collapse and death often with convulsions in which no anatomical evidence of hemorrhage or edema can be discovered post mortem The reported cases are not numerous but most clinicians of large experience have met with this unfortunate accident Leichtenstern[29] states that the collapse may come on during aspiration more often soon after aspiration or may develop during irrigation of the cavity with antiseptic solutions He analyzes twenty three fatal cases in the literature Fox[30] reports twelve instances of fatal syncope all without pathological lesions adequate to explain the complication

The three fatalities described by Russell[31] were all in children with pneumonia His explanation of the phenomenon is that the needle traumatizes the vagus nerve endings in the lung tissue thereby setting up reflex disturbances of the heart He considers the reflex as pulmonary rather than pleural but other observers usually have failed to find a wounded lung in their necropsies Moreover by this hypothesis one cannot explain similar instances of collapse during irrigation

Recently many of these accidents have been ascribed to air embolism[32] and in a few cases such emboli have been found in the coronary and cerebral vessels at autopsy Schlaepfer[33] has shown experimentally that an extremely small quantity of air introduced into the pulmonary vein may cause death Undoubtedly this mechanism explains certain of these cases but obviously it fails to explain the great majority for several reasons[34] First syncope occurs most frequently in simple exploratory puncture where no air is introduced Second syncope rarely is encountered in the production of artificial pneumothorax Finally air emboli cannot be found at the post mortem examination in most instances

Our interest in the subject was aroused by the collapse of a patient with pleural effusion within a few seconds after the puncture when only a few ounces of fluid had escaped The post mortem showed no laceration of the lung no hemorrhage or edema no air emboli and no lesion in the brain Animal experiments show that although the healthy pleura is tolerant of irritation the *inflamed* pleura may react to irritation whether mechanical or chemical by marked reflex circulatory disturbances Schlaepfer[33] states that he was unable to confirm these findings but his experiments were done on the normal pleura The pleural reflex may act on the cardio inhibitory fibers of the heart through the vagus nerve endings or on the vasomotor centers through the sympathetic nerves Clinically we have often observed a transitory fall in the arterial pressure coincident with the needle thrust especially when much force is used This is due apparently to a direct inhibition of the heart action and usually is quite transitory The effect is exaggerated in the yielding chest of children or when the effusion is massive and the cardiac action already embarrassed We also were able during thoracentesis by scratching the pleura to induce a fall in blood pressure even to the point of faintness

Our conclusions based on these experiments were as follows (1) Syncope occurring during the act of puncture is the result of direct cardiac inhibition (2) Syncope during aspiration results from irritation of the pleural or pulmonary nerves either by the trocar or by congestion It is most common toward the end of the operation when the instrument is most likely to scratch the pleura and when the lung is most congested (3) Syncope occurring within forty eight hours after aspiration probably is due to the circulatory reflexes arising from congestion of the lungs (4) Syncope during irrigation of the pleural cavity is the result of a reflex arising from the chemical irritation of the pleura

The prevention of collapse should be directed toward these ends (1) Avoid unnecessary force in penetrating the chest wall especially in children and the debilitated A dull trocar often is at fault (2) Avoid irritation of the pleura as far as possible See that the needle swings free and if it strikes the lung during respiration change the position A trocar canula is less likely to irritate the pleura than a needle (3) Regulate the aspiration in such a way as to produce the least congestion Evacuate slowly use only moderate suction and do not remove over 1 500 c c of fluid (4) *In irrigation of the cavity do not use irritating chemicals* and see that the rubber drainage tube does not scratch the pleura

Therapeutic Introduction of Air After Aspiration — The harmlessness of air accidentally entering the pleural cavity during thoracentesis has been commented upon already It has been suggested by Achard[35]

and others that sterile air can be introduced advantageously after evacuation to replace partially the fluid. By this method he succeeded in drawing off three or four liters with safety. A more important purpose in substituting an air cushion in place of the heavier effusion is to avert the excessive congestion of the lungs. The air is absorbed much more rapidly than the fluid and allows a gradual expansion of the retracted lung. It seems rational to suppose that edema and circulatory disturbances would be mitigated by this procedure. We have never seen infection take place from introducing air filtered through cotton. The amount of air admitted should be relatively small, never exceeding one third of the quantity of fluid evacuated. The use of air to prevent re-accumulation of fluid has been advocated by some writers. A more satisfactory method recently described is the use of olive oil or gomenol[12].

End Results. A perfect recovery means complete replacement of dislocated viscera, recovery of normal lung expansion and free mobility of the diaphragm. In favorable cases the fluid ceases to accumulate after one or two tappings and the lung recovers its full function. When, however, thoracentesis is long delayed, adhesions may form to such an extent that the affected lung expands only partially. Much may be accomplished in the after-treatment by the daily practice of breathing exercise, by active out-of-door life and good nourishing food. For years afterward, however, one may expect to find over the affected side relative dullness and more or less impairment of the vesicular respiration.

EMPYEMA

Empyema is a pleurisy with purulent effusion.

Etiology

The exudate may be purulent from the beginning, but usually it starts as a seropurulent effusion and gradually acquires a thicker consistency as the pus cells increase. The pneumococcus and streptococcus are the common etiological germs found in the exudate. According to most observers the pneumococcus is the causative organism in about half of all cases in hospital practice. Lord, in his series of empyemas, found streptococcus in 39.4 per cent, pneumococcus in 20.4 per cent, staphylococcus in 3.6 per cent, and mixed infections in 16 per cent. The pus was sterile in 18 per cent and many of this group were tuberculous. But during the world war period the statistics show a predominance of the streptococcus. The great epidemics of measles, influenza and streptococcus pneumonia

were associated with an overwhelming proportion of streptococcus empyemas. The tubercle bacillus not infrequently is responsible for a purulent exudate, especially in the type where no organisms are present. Many tuberculous pleurisies become purulent after the secondary invasion of pyogenic cocci. Occasionally the influenza bacillus, staphylococcus, actinomyces and Friedlander's bacillus are found in the pus. Empyema generally is a complication of some pulmonary inflammation. Lobar pneumonia, bronchopneumonia, abscess of the lung and tuberculosis are the chief primary diseases. In military practice penetrating wounds of the chest contribute a fair share of the cases.

Pathology

Associated with lobar pneumonia there is nearly always a thick fibrinous exudate in which leucocytes and pneumococci abound. Empyema often springs from this soil and the pus is thick, creamy and has a peculiar greenish color. The pus in streptococcus and tuberculous empyema is thinner and contains fewer formed elements. In actinomycosis the pus is thick and in it are found the characteristic granules.

A purulent exudate in the chest works far more damage to the viscera than a serous effusion. The intense inflammation of the pleural surfaces brings about early organization of the fibrinous exudate and the formation of thick firm adhesions. After a time the retracted lung is incapable of expansion even when the pressure is removed by operation. Likewise the adhesions to the mediastinum tend to fix permanently the heart in its displaced position. According to Norris and Landis, prolonged compression of the lung by pyothorax is one of the common causes of localized pulmonary fibrosis. Similar changes take place in the pleural covering of the diaphragm, leading to loss of mobility and deformity.

Spontaneous absorption may take place in small collections of pus. When a large accumulation is left to nature, septicemia ensues. Exceptionally pus may be so completely walled off that absorption is slow and the patient lives to develop amyloid changes in the kidney, liver and spleen. A neglected empyema occasionally secures an outlet by perforation through the lung, draining into the bronchial tubes or through the chest wall.

Symptoms of Empyema

During the course of a lobar pneumonia the presence of pus is first suspected by the persistence of fever after the crisis seems to have passed.

The morning temperature may fall but day by day the evening temperature is high Dyspnea may have disappeared but the pulse rate remains rapid the patient acquires a pale sallow color, perspires freely and loses weight The streptococcus empyemas complicating influenza pneumonias have an earlier onset and cannot be apprehended readily by the symptoms as they are practically the same for both conditions

Leucocytosis is the rule in pneumococcus empyema and in streptococcus empyema following measles or abscess of the lung In the influenza bronchopneumonias however a normal or low leucocyte count is present in the majority of cases and the development of empyema seems to have no constant influence on the white corpuscles

Physical Signs of Empyema

The detection of pyothorax is more difficult than that of serous effusions for the latter usually is a primary condition while the former generally is associated with some form of inflammation of the lung A simple empyema exhibits physical findings very similar to those of serous effusion But the numerous cases of metapneumonic empyema give rise to the most protean manifestations owing to the fact that the pus is superimposed upon a profoundly altered lung tissue The early recognition of empyema demands the greatest skill study and experience on the part of the clinician A final diagnosis is not always possible by the older methods of examination The x ray has proved of great assistance in the localization of pus especially when it is encapsulated or situated between the lobes Exploratory puncture must also be looked upon as one of the legitimate and most valuable diagnostic procedures

The appearance of the patient after the empyema has been present for some time is that of sepsis The affected side is more or less crippled in its respiratory movements and the diaphragm shadow cannot be seen Bulging of the interspaces with slight edema of the chest wall often can be demonstrated especially in children and thin individuals When the abscess points there is a localized bulging and later a fistulous opening the so called empyema necessitatis

Pulsating empyema is not a rare condition and is nearly always on the left side (Sailer[36]) The cardiac pulsations are transmitted through the adjacent fluid Displacement of the apex impulse is common with these larger effusions A late manifestation of chronic empyema is clubbing of the fingers which according to Norris disappears after the pus is evacuated

By the sense of touch the levelling of the interspaces and the abnormal position of the apex beat may be perceived Tenderness to pressure over

the inflamed area is a sign of value and is attributed to a neuritis of the intercostal nerves Empyema tends to impair or to destroy the tactile fremitus

There is no essential difference in the percussion note over an exudate of serum and of pus except possibly that the flatness is more marked in the latter As in serous effusions the vesicular sounds usually are lost and the voice sounds distant and diminished in intensity But the frequency of bronchophony over areas where the lung is adherent to the chest wall makes one conservative in the interpretation of auscultatory evidence Often it is impossible by means of the stethoscope to differentiate between consolidation and empyema Baccelli s sign the transmission of the whispered voice through serous fluid and failure of transmission through pu has proved to be unreliable

Diagnosis of Empyema

The signs of pleural effusion have been described already The purulent character of the exudate is apprehended by the development or continuance of fever anemia and sepsis Coming in the wake of croupous pneumonia empyema commonly is mistaken for delayed resolution of the lung a presumption that can only be justified after repeated efforts have been made to eliminate the presence of pus

The Roentgen ray has become established as a method quite as valuable as percussion and auscultation in the diagnosis of empyema Its peculiar field of usefulness is in the localization of encapsulated pus pockets that are too deep for recognition by sound variations These atypical forms will be described separately

Time and experience have shown that the diagnosis of empyema must be determined not by any pathognomonic signs but by a correlation of the evidence obtained by all these methods Even puncture may be misleading for a dry tap does not exclude the presence of pus

Military Experience With Empyema

During the war empyema assumed the rank of first importance among medical problems The great prevalence of the disease its unique and variable character and its heavy contribution to mortality have made i the subject of numerous studies and make necessary a somewhat detailed description For the voluminous literature on the subject the reader is referred to Progressive Medicine[37] the Reports of the Empyema Commission[38] and to the article of Vaughan[39]

Empyema complicating the ordinary croupous pneumonia presented in the main the same clinical picture with which we are familiar in civil practice and needs no special comment The unusual features of the empyemas in military service were due to the unprecedented epidemics first of measles second of streptococcus infections and finally of influenza Broncho pneumonia in all three outbreaks was the prevailing pulmonary complication exhibiting the greatest variety of anatomical lesions As sociated with these pneumonias were empyemas equally atypical in location onset and in their clinical course The pus almost always was caused by the streptococcus and the variations in type were attributed largely to the factors of virulence as influenced by the initial infection and by the susceptibility of the host

During the first years of mobilization measles and streptococcus infections of the respiratory tract were rife Three periods stand out as distinctive in the virulence of the lung and pleural complications

The first period from November to January 1918 inclusive represented the maximum intensity of the infection Following measles the patient developed dyspnea fever and cyanosis The lung became edematous and a serous or seropurulent fluid escaped into the pleural cavity This effusion abounded in streptococci and the organisms were present in blood cultures A fatal termination often supervened before the lung was consolidated and before the exudate was purulent Aspiration or surgical incision had little or no influence in retarding the fulminating infection and even may have been detrimental Some patients survived this stage and developed true consolidation and empyema as well as abscess of the lung Surgical intervention then was indicated but might fail to drain all the pus pockets

The second period during the winter months showed a less virulent and less stormy infection Consolidation and abscess of the lung were common and the effusion at first serous became thick and purulent after an interval of several days Metastatic effusions often developed in the pericardium and joints and multiple abscesses appeared in the skin The mortality still was formidable but far less than in the first period

The third period in the spring months was milder in every respect Empyema was slow in its formation and was responsive to treatment by aspiration and incision The infection seemed to have become attenuated and most patients survived

Empyema following influenza was a feature of the great epidemic in the fall of 1919 Here again we saw at the beginning of the outbreak an infection of overwhelming virulence in which the patient was likely to die before consolidation was advanced and before the streptococcus effusion

had become thickly purulent Aspiration or incision both failed to retard the unfavorable progress of the infection A few weeks later the influenza virulence underwent a transformation and the intoxication was less severe There was time for the gradual pneumonic progression from congestion to consolidation and for the leisurely conversion of the seropurulent pleural exudate into pus Measures for the removal of the fluid whether aspiration or thoracotomy now were helpful

Treatment of Empyema

A consideration of the phenomena of virulency just described readily explains the heated discussions for and against early tapping and the relative merits of thoracentesis and thoracotomy The great divergence of mortality statistics usually ascribed to this or that method of treatment is in reality due for the most part to varying stages of virulency of infection In hospitals where the same method was followed continuously the mortality was high in the early virulent period and low in the later mild periods The condition of the patient is quite as important as the disease in deciding upon therapeutic methods

Certain fundamental physiological principle have however emerged from the work stimulated by the experiences of World War I Graham[3] has shown that the size of the pleural opening compatible with life is dependent on the vital capacity provided the mediastinum is not fixed This of course may not hold where an opening is made into a walled-off empyema cavity but it does explain the dangers involved in open drainage of a pleural effusion during the active stage of pneumonia Particularly in diffuse and generalized pulmonary involvement such as occurs in streptococcus pneumonia the vital capacity is extremely low and any further decrease such as that caused by open drainage with the resulting pneumothorax may result in death from asphyxiation Early thoracotomy in these cases is a dangerous practice Aspiration with the needle or trocar can be performed repeatedly with very little discomfort to the patient When the pneumonia has resolved and the vital capacity as well as the general condition of the patient has improved then thoracotomy is advisable if pus still persists At this stage the empyema frequently becomes walled off and this further diminishes the dangers of operation Occasionally small pneumococcus empyemas are well drained with complete recovery by aspiration alone but in the vast majority of cases the treatment should be turned over to the surgeon

Pus Pockets — Streptococcus infections are prone to form multiple pockets of pus in the pleural cavity as a result of adhesions These pockets present great difficulties in drainage requiring aspiration at different localities as often they are not confluent After thoracotomy the operator may be compelled to break up the adhesions to establish free drainage

Irrigation of the chest cavity following operation has been both praised and condemned by surgeons Dakin's solution has been used quite extensively with varying results It is well in this connection to call attention to the accidents sometimes arising in the course of irrigation Convulsions with syncope have been described by Weil[10] Janeway[11] observed a transitory paralysis on two occasions while injecting a solution of hydrogen peroxide Following the introduction of a two per cent solution of formalin and glycerin Billings[4] reports a case of collapse and death One case of sudden death while introducing Dakin's solution, has come to our attention Fatal syncope has followed the rather forceful adjustment of the drainage tube

The cause of this syncope has been explained by Lewis and the senior author[12] as a circulatory reflex arising from irritation of the sensitive inflamed pleura The pleural membranes in advanced empyema are protected by a fibrinous exudate so that the pleural reflex is not often encountered but the exposure of a pleural membrane in the early stage of empyema to traumatic irritation not infrequently sets up a circulatory reflex that may be fraught with danger This reflex is less likely to occur if the patient is lying down

Specific Therapy — The introduction of the sulfa drugs and antibiotics has dramatically changed the treatment and prognosis of empyema The sulfonamid drugs have reduced the incidence of empyema following pneumonia from about 5 per cent to 1 per cent However the sulfonamides have not been successful in the treatment of empyema itself

Once the pleuritic fluid becomes turbid from pus formation penicillin should be used[63] The parenteral administration of penicillin was investigated by Fatti Florey and associates[64] who found that the drug penetrated the pleural cavity, that toxic symptoms disappeared and the convalescent period shortened

However, the direct injection of penicillin into the pleural cavity in combination with aspiration gives the best results Penicillin is effective in combatting pneumococcus hemolytic streptococcus staphylococcus and the fusiform spirochetes It is not reliable in the treatment of the rarer gram negative infections such as influenza tularemia and Friedlander's bacillus

For this latter group favorable reports have been reported from the use of streptomycin[65] Penicillin when injected into the pleural cavity diffuses into the blood stream slowly and remains present for from 1 to 3 days Brown and associates report that by the combined method of aspiration and intrapleural injection 50 to 65 per cent of pneumococcus and staphylococcus infections were completely cured without surgical intervention The cases of putrid empyema with mixed infections usually demanded surgical drainage[6]

It is advisable to begin the penicillin injections early before the pus thickens otherwise pockets may be formed that are not permeated by the drug The usual dosage is 50 000 to 100 000 units injected after aspiration at intervals of 24 to 48 hours until the pus becomes sterile Three or four injections ordinarily are sufficient In stubborn cases the treatment may be reinforced by intramuscular injections The staphylococcus infections require a much longer period of treatment than the pneumococcus and streptococcus types

Empyema in actinomycosis generally is secondary to a lung infection The pus is destructive of tissue and tends to perforate the chest wall The pus contains small granules which show under the microscope the characteristic threads and club shaped bodies Free evacuation should be performed and iodide of potash administered internally The drug should be given to tolerance or until improvement is noted In spite of treatment these cases tend to form chronic suppurating sinuses and to terminate in amyloid degeneration of the viscera

Primary Atypical or Virus Pleurisy

Since the last World War the typical lobar pneumonia due to pneumococcus has become less frequent In its place a new type of lung infection has appeared the primary atypical or virus pneumonia Pleurisy dry or with effusion may complicate the pneumonitis Aspiration may be indicated No specific therapy is effective unless aureomycin should be so regarded it is worthy of trial when evidence of secondary coccus infection is lacking Penicillin should be employed if there is evidence of pus formation from a secondary coccus infection[67]

In lupus erythematosus disseminatus the occurrence of pleurisy is common In periarteritis nodosa only a small percentage of patients develop pleurisy

Diaphragmatic Pleurisy

The symptoms and signs of diaphragmatic pleurisy are entirely unlike those of parietal pleurisy and often are characteristic By most writers it is treated as a rare type but in our experience it is of frequent occurrence and is either overlooked or the findings are misinterpreted Diaphragmatic pleurisy may begin and end in a small localized area giving no auscultatory signs whatever of its presence Its recognition then depends

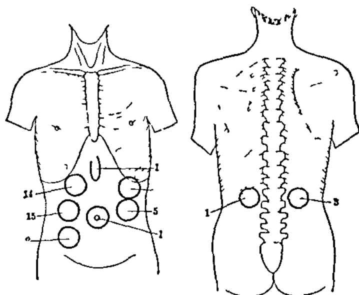


FIG 4 — Points of maximum pain and tenderness in abdomen and back occurring in ninety three cases of diaphragmatic pleurisy

on the location of referred pain and on the x ray revelation of adhesions between the diaphragm and lower lobe The condition is found most commonly however in pneumonia of the lower lobes and in extensive pleurisy of the lower thorax In a series of 93 cases including those previously reported by the senior author 57 of the patients had a lower lobe pneumonia with pleurisy and 36 had pleurisy alone In 47 the pleurisy was situated on the right side in 35 on the left and in 1 was bilateral The diagnosis in most instances was made evident by physical findings in the thorax in 8 instances confirmed by autopsy and in 6 instances abdominal disease was excluded by exploratory laparotomy

Pain referred to parts distant from the seat of inflammation was the outstanding symptom in these cases Referred abdominal pain was present in 64 cases in all cases involving the upper quadrant (7 to 10 dorsal

segments) and in 27 cases the lower quadrant as well (10 to 12 dorsal segments) Bilateral pain in the belly was noted four times The pain usually was spontaneous and with it was tenderness to pressure Hyperesthesia and hyperalgesia of the skin were almost constant and showed a decided tendency to follow band like areas corresponding to different spinal segments Over this sensitive area the musculocutaneous reflexes were exaggerated and often the wall remained in a state of rigidity

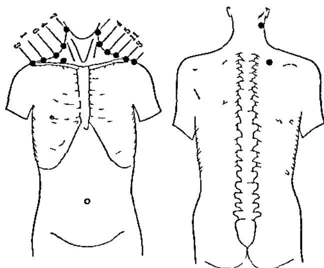


FIG 5 — Points of maximum pain and tenderness in the neck region occurring in *ninety three cases of diaphragmatic pleurisy*

The maximum point of pain and tenderness to pressure was especially studied (Fig 4) This point was located (a) in the gall bladder region 14 times (b) lateral to and slightly above the navel 20 times (c) near McBurney s point 2 times (d) over the navel 1 time (e) midepigastrium 1 time (f) splenic region 2 times (g) lumbar region 4 times

Referred neck pain occurred in 62 cases or in a little more than two thirds of the total The pain was located by the great majority of patients along the trapezius ridge occasionally over the shoulder cap and in the supraclavicular space (Fig 5) All of these areas are supplied with sensory nerves from the third and fourth cervical spinal segments The pain usually was spontaneous and of sharp stabbing character always well localized by the patient with the tip of his finger Pressure over this point often was very painful The skin and subcutaneous tissues in the immediate neighborhood showed the same hyperalgesia and hyperesthesia

as were found over the abdomen but the point of maximum pain and tenderness in the neck was sharply localized and more constant The exact locations of maximum pain points in the neck are illustrated in Fig 5

Kelly and Weiss[43] found a common area of tenderness over the twelfth rib posteriorly occurring 17 times in 22 cases of diaphragmatic pleurisy

Factors Influencing Pain in Diaphragmatic Pleurisy — The appearance of referred pains in the abdomen or neck generally was early in the course of the disease More often abdominal pain preceded the neck pain when both were present The duration of the pain and tenderness varied in much the same way as in parietal pleurisy Sometimes the pain disappeared after a few hours as a rule it persisted one to three days and occasionally over a week The pain nearly always was induced or aggravated by cough and deep inspiration especially during the acute stage

Measures limiting the excursion of the diaphragm on the affected side such as lying on the painful side or tight pressure of an abdominal band often give relief Some patients secured ease by lying doubled up on the affected side with the shoulder held down by a pillow

The abdominal pain was associated with a maximum point of pain and tenderness far more frequently on the right than on the left side Such a point was observed in 31 out of 47 cases on the right side or 66 per cent while it was noted in only 7 out of 35 cases on the left side or 20 per cent In contrast to this disparity the neck pain occurred with almost equal frequency on the two sides Tenderness of the phrenic nerve a symptom emphasized by many writers was found in but one case and that was doubtful Vomiting was present in 17 cases and often was responsible for a mistaken diagnosis of abdominal inflammation Hiccough another symptom supposed to be common in diaphragmatic pleurisy was noted in only 6 cases being unusually severe however in 3

Differential Diagnosis of Diaphragmatic Pleurisy — Appendicitis was incorrectly diagnosed in 9 cases Two of these were operated upon and the abdominal viscera found to be normal Cholecystitis was diagnosed in 8 instances 2 of which came to laparotomy without discovering any pathological condition of the gall bladder or the neighboring structures Ulcer of the stomach with perforation was twice diagnosed and once operated upon without discovering any lesion in the belly Liver absces was diagnosed in two patients One was opened up with negative results The other mistaken diagnoses included one instance each of peritonitis renal calculus infectious lumbago and brachial neuritis

The main points of differentiation between diaphragmatic pleurisy and inflammation of the abdominal viscera are as follows

1 In referred pleural pain the skin and muscles of the abdomen are *more sensitive to pain and touch than in visceral disease This is best* elicited by pinching of the wall and scratching of the skin

2 In referred pain the cutaneous reflexes are more lively than in visceral disease as a rule

3 Deep pressure with the flat surface of the fingers is well borne in referred diaphragmatic pleural pain while it elicits a dull deep pain when applied over the inflamed organ e g an appendix or gall bladder

4 Evidences of respiratory infection usually are present in diaphragmatic pleurisy such as cough expectoration herpes of lip sore throat high leucocytosis rapid respiration etc

5 Appearance of a sharp definitely localized pain in the neck on the same side as the abdominal pain often reveals the true condition since it points to irritation of the phrenic nerve

6 The referred pains in the neck and abdomen usually are induced or aggravated by cough and deep inspiration

7 Nausea and vomiting are more constant in visceral abdominal inflammation but may occur and be very pronounced also in diaphragmatic pleurisy

8 The x ray may show a deformity of the upper surface of the diaphragm from pleural adhesions

9 Hiccough is not a common symptom in diaphragmatic pleurisy *contrary to the current belief It was present only 6 times in our series of* 93 cases It is seen more often in visceral diseases of the abdomen than in diaphragmatic pleurisy

Subphrenic Inflammation

In the study of pain distribution from subphrenic inflammation we are greatly handicapped The opportunities for experimental irritation of the under surface of the diaphragm in human beings are rare Moreover the existence of abdominal pain in the course of subphrenic inflammation may be properly attributed to associated inflammation of the abdominal viscera Only in those cases in which definite sharply localized pain and tenderness develop in the neck or shoulder region can we be sure that the diaphragm is involved We have observed 6 cases of subphrenic inflammation exhibiting neck pain 3 on the left and 3 on the right The painful point is in every respect identical with the referred pain in diaphragmatic pleurisy

Mediastinal Pleurisy

A dry fibrinous exudate in the region of the mediastinum is of no special importance and cannot be recognized clinically It is only when there is an encapsulated exudate present that the diagnosis is desirable or possible A convenient anatomical classification is that employed by Frick[1] in his excellent article on the subject which in substance is quoted

1 Pleuritis mediastinalis anterior sinistra in which the effusion is located in front of the left pulmonary peduncle The fluid may extend along the upper mediastinal pleura or downward to the diaphragm and outward to the parietal pleura It seldom extends to the posterior mediastinum The symptoms that are distinctive are pain under the sternum or between the sternum and nipple Dyspnea is proportionate to the pain Cyanosis is conspicuous only in the large effusions The chief physical signs are flatness beyond the cardiac dullness obscuration of the apex beat and occasionally a bulging of the precordium The condition usually is confused with pericardial effusion or a suppurative mediastinitis The x ray may be of assistance by revealing a shadow contour unlike that of pericarditis

2 Pleuritis mediastinalis anterior dextra may give rise to substernal pain similar to that described in the sinistra but the pain tends to extend to the right nipple Cyanosis is encountered more frequently on the right because of the pressure on the superior vena cava Flatness is present a varying distance to the right of the sternum

3 Pleuritis mediastinalis posterior always is situated on the left or right of the mediastinum but the manifestations are the same in either case The process may give no symptoms whatever except those of septic absorption In other instances the effects of pressure on various structures are seen paroxysmal cough from pressure on the vagus nerve dyspnea edema of the larynx and hoarseness from pressure on the trachea dysphagia from pressure on the esophagus dilatation of the thoracic veins from pressure on the azygos veins Pain is exceptional although there may be a region of tenderness near the spine The posterior location is more common than the anterior

A typical case of the author s is shown in Fig 10 Following a bronchopneumonia of the left lower lobe the patient ran a septic temperature with a marked leucocytosis and a daily expectoration of a moderate quantity of sputum containing pus cells and pneumococci The tentative diagnosis of unresolved pneumonia was abandoned after the restoration of normal lung findings There was no pain but slight tenderness over

the lower thorax near the spine The x ray showed a penumbra about the heart shadow from the antero posterior view (Fig 10) The lateral exposure marked out the outline of a bulging mass close to the spine and quite distinct from the pericardium (Fig 11) Upon this evidence a needle was inserted in the eighth space posteriorly inside the scapular line and directed forward and toward the median line A few drops of thick

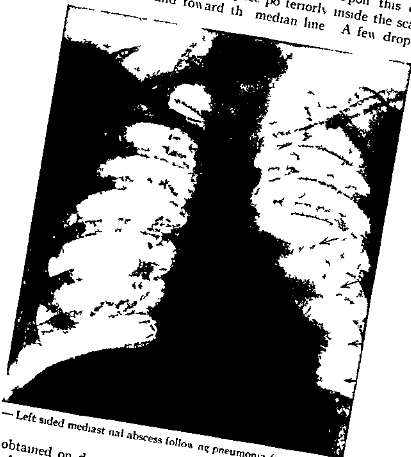


Fig 10 — Left sided mediastinal abscess following pneumonia (antero posterior view)

pus were obtained on deep penetration The surgeon incised the wall at this point followed the needle track with long hemostatic forceps dilated the opening and inserted a rubber tube Drainage of pus continued for several days until the leucocytosis disappeared and the x ray showed no mediastinal shadow Recovery was complete

In all varieties of mediastinal exudates the x ray is indispensable Fluroscopic examination will exhibit a pulsation of the tumor in aneur

visceral pleura Spontaneous emphysema under the skin has been a rare complication of pneumonia in the past But during the war time in fluenza epidemic many cases were reported from military hospitals as coming on during the acute stage of bronchopneumonia The peculiar crepitation and edema appear first in the subcutaneous tissues of the neck and upper chest spreading to the face and arms and often to the abdo men Pneumothorax is exceptional

The sputum exhibits a variety of organisms Berkeley and Coffen[16] found in a series of 21 cases type IV pneumococci in 9 non hemolytic streptococci in 8 influenza bacilli in 3 and tubercle bacilli in 1 case They describe two routes by which the air escapes from the lung into the sub cutaneous tissues (1) The intrapleural route by which the air passes through both visceral and parietal pleuræ Pneumothorax may occur but if adhesions are present the air may not enter the pleural cavity (2) The extrapleural route At autopsy a rupture of an air sac in the peripleural borders of the lung may be found with excavations of air covered by tense pleural membrane From this point ' air streaks follow the blood vessels to the hilus into the posterior mediastinum Thence the air dissects its way into the superior mediastinum and enters the subcutaneous tissues in the neck

The prognosis naturally is more grave as a result of this complication but many cases recover No special treatment is indicated

Non Inflammatory Fluids in the Pleural Cavity

Hydrothorax

Hydrothorax is a clear serous non inflammatory effusion in the pleural cavity The fluid is a transudate as distinguished from the exu date of pleurisy Hydrothorax usually is a feature of a general dropsy and consequently is associated most often with cardiac and renal disease The immediate cause is to be found in a decreased osmotic pressure of the blood or in an increased pressure in the veins draining the pleura or both

The transudate from a decompensated heart may be unilateral and in that event has a decided predilection for the right side of the chest or bilateral with a greater amount of fluid in the right pleural cavity The reason for the relative frequency of right sided effusions is not entirely clear but some recent observations of Wood and Wolferth[17] are enlight ening They found that most cardiac patients actually lie most of the time on their right side because of annoying or even alarming symptoms caused by lying on the left side X ray observations showed that there was considerable shifting of large hearts with changes in position so that the

right sided effusions could be produced readily by pressure on the right pulmonary veins[48] or by purely hydrostatic factors[49] Good evidence against Stengel's[50] theory that pressure on the azygos major vein was responsible has been offered by Fetterolf and Landis[45] A further factor in cardiac effusions is the rather frequent presence of low serum protein in the blood[51]

Hydrothorax from renal disease generally is bilateral A bilateral transudate may complicate pernicious anemia leukemia or cachectic states Other causes of hydrothorax usually unilateral are thoracic *tumors which produce venous obstruction such as carcinoma mediastinal* glands and aneurysms Cirrhosis of the liver may be associated also with a pleural transudate

Symptoms — Since hydrothorax is not a disease entity the constitutional symptoms are those associated with the basal process The onset usually is insidious and is overlooked unless routine examinations of the chest are made in cardiac and renal diseases Pain is absent and there *is no fever attributable to the effusion The tendency of hydrothorax is* to produce dyspnea but this may have preexisted as a result of the kidney or heart affection Increasing dyspnea at any rate should impel one to examine the thorax frequently for fluid

There is no friction sound and the fluid being unrestricted by adhesions is more moveable than that of pleural exudate In other respects the findings are similar to those described in pleurisy with effusion

Edema of the lungs may cause enough dullness at the base to be a source of confusion The x ray is useful in certain cases in demonstrating fluid Thoracentesis is however the simplest method of clinching the diagnosis The fluid is clear of low specific gravity 1 004 to 1 015 and contains few cells Cultures are sterile

Successful control of the general dropsy by cardiac stimulants diuretics and purgation will bring about the absorption of a moderate hydrothorax Should the accumulation be large it is advisable to aspirate The relief of dyspnea often is astonishing and may be the turning point in the restoration of the cardiovascular balance A limitation of the liquid intake to 1 000 c c per diem is serviceable in delaying or preventing the return of the fluid When low serum proteins are a factor in non renal cases a high protein diet may be valuable

Hemothorax

Hemothorax is an effusion of blood in the pleural cavity Hemothorax is distinct from the inflammatory hemorrhagic exudate The

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The breath sounds are faint, distant or suppressed. The voice is distant or nasal (egophony). When air or gas is present, succussion sounds may be obtained. When the aspirating trocar is used the blood usually flows out readily and shows little tendency to clot. After a few days have *elapsed in the traumatic cases, pus cells and various bacteria often are* mixed with the blood.

The sudden development of dyspnea, air hunger, anemia and shock without pain and without fever, is suggestive of hemorrhage. Pneumo*thorax is the only other thoracic condition that is capable of simulating* these symptoms. Physical examination and exploratory puncture will confirm the diagnosis. In the presence of a penetrating chest wound the complication of pneumothorax is always to be looked for and requires *differentiation only from pleurisy with effusion.* Especially *in hemothorax* which is associated with spontaneous pneumothorax, severe abdominal pain may lead to a false diagnosis of an acute surgical condition of the abdomen.

Treatment of Hemothorax.—*Any treatment is likely to be unavailing* in hemothorax from the rupture of aneurysm. Smaller collections of blood accompanying tumors should be treated conservatively. It is well to bear in mind that the chest wall as well as the weight of the fluid offers considerable *resistance to the bleeding vessels.* Premature evacuation removes the compression and may encourage further hemorrhage. Massive accumulations demand the withdrawal of a part of the fluid to forestall fatal syncope. In such cases the introduction of air in moderate quantity into the pleural space serves to lessen the engorgement of the thoracic blood vessels.

Traumatic hemothorax should be under the care of a surgeon. The report of the Research Laboratory of the American Expeditionary Forces[40] on intrathoracic surgery emphasizes the following points:

1. Simple hemothorax limited in amount and without symptoms should be treated expectantly. When signs of a rapid increase in amount *or of infection develop,* radical treatment is indicated. *If the hemothorax* is large, and particularly when dense clots are demonstrable fluoroscopically, radical treatment promises earlier and more complete recovery with slight if any increased danger. The decision as to the treatment of *moderately extensive hemothorax must depend on many factors,* preference being given to conservation.

2. Hemothorax with symptoms of acute anemia and continued bleeding demands measures to obtain immediate hemostasis, the safeguarding against secondary hemorrhage, blood transfusion and when possible, repair according to established principles.

source of hemorrhage in the pleural cavity is from the rupture of a thoracic blood vessel or of an intercostal artery. The bleeding may be spontaneous or traumatic.

1. Spontaneous hemothorax in the majority of instances follows the rupture of an aortic aneurysm. The blood usually escapes into the left pleural cavity and may fill that side of the chest completely. Less frequently an abscess of the lung causes erosion and bleeding from a small thoracic artery. Rupture of varicose veins created by the presence of cancer or other tumors is the occasional starting point of hemorrhage. Rarely bleeding is associated with a spontaneous pneumothorax.

2. Traumatic hemorrhage is more common than the spontaneous form but it is of more interest to the surgeon than to the internist. All perforating wounds of the chest are likely to produce more or less bleeding in the pleural cavity because of the exposed position of the intercostal arteries. Injury to the thoracic vessels from penetration of the lung does not necessarily cause hemorrhage provided the larger vessels are not implicated. A bullet wound may penetrate the lung without causing any serious damage. Murphy[5] states that hemothorax occurs in sixty to seventy per cent of penetrating bullet wounds as a result of laceration of the intercostal arteries. The bleeding often is slow and continuous and if the patient is moved about there is great danger of secondary hemorrhage.

Symptoms and Signs of Hemothorax. — The accumulation of blood in the pleural cavity produces dyspnea and pressure symptoms in proportion to the amount present. In addition to the mechanical disturbances there is anemia from the loss of blood and often air hunger. After penetrating shell wounds in battle the patient is in a condition of shock which is a consequence of concussion as well as of hemorrhage. The pulse is weak and the skin moist from profuse perspiration. Fever sets in within two or three days in the larger accumulations.

Infection is a frequent complication of traumatic hemothorax and is manifested by symptoms of progressive sepsis and irregular fever more pronounced than in uncomplicated cases. Leucocytosis is moderate after considerable hemorrhage and usually high following pyogenic infection.

The presence of blood in large amount obliterates the intercostal depressions and immobilizes the affected side. The displacement of the heart is quite constant. Tactile fremitus is lost more completely than in serous effusions. Percussion elicits a dull or flat note over the fluid. Shifting of the dullness on changing position often is observed. The tympanitic note of pneumothorax over the fluid level may be present signifying either the entrance of air or the formation of gas from anaerobic organisms.

Pneumothorax

Etiology

Air or gas may gain entrance into the pleural spaces by several routes (1) through an opening in the thoracic wall by way of the aspirating needle or of penetrating wounds (2) through a break in the visceral pleura and alveoli of the lung (3) through a fistulous communication with the alimentary tract (4) by the formation of gas on the part of anaerobic bacteria present in the cavity

It is apparent that an opening which permits access of air from an *infected lung or hollow viscera or from outside the chest wall through a dirty wound is likely to admit bacteria at the same time Consequently infective pleuritis is the usual sequel of pneumothorax and an effusion* either serous (seropneumothorax) or purulent (pyopneumothorax) may be expected Even the escape of air from a non infected lung or the introduction of air through a clear opening in the chest wall tend to excite a pleural exudate in certain cases Air injected into a healthy pleural cavity rarely excites effusion But when the pleura is inflamed as in dry tuberculous pleurisy air may induce a serous outpouring

Pneumothorax occurring accidentally during aspiration of pleural effusions is encountered frequently A careful examination of the chest the day after tapping often reveals above the fluid level a circumscribed area of tympany or even succussion sounds A slight leak *in the connections of the aspirating apparatus may admit the air or when the canula is cleaned out with a stylet an opportunity is* given for air to enter especially toward the end of aspiration when there is a strong negative intrapleural pressure The air is absorbed in a day or two and does no harm The introduction of air for therapeutic purposes will be referred to later

Perforating wounds of the chest frequently lead to pneumothorax A bullet wound may go through the chest wall and lung without causing pneumothorax But many bullet wounds and practically all penetrating shell injuries are followed by pneumothorax In external pneumothorax the wound may be closed or may be open allowing continuous entrance of air *The first efforts of the surgeon are to close the perforation Infection of the cavity and pleuritic effusion are almost constantly a sequel in* this group of cases

Perforation of the visceral pleura and lung by a sudden rent of the visceral pleura is responsible for a large number of cases of pneumothorax It results from the erosion and rupture of the outer surface of the lung in tuberculosis pulmonary abscess and gangrene bronchiectasis and pleural

3 Hemothorax with symptoms of respiratory and circulatory embarrassment due to pressure offers a better chance of recovery if immediate surgical care is given including accurate hemostasis and repair of visceral injuries

4 Through and through chest wounds from bullets or shell fragments in the absence of the above symptoms are non operative types under ordinary conditions and always so under battle pressure For the failing circulation of exsanguinated patients transfusion of blood is of value and should be carried out promptly if proper facilities are available When a donor is not available normal salt or the gum salt solution may be employed

Chylothorax

A milky fluid in the pleural cavity is termed chylothorax Three types of chylothorax are distinguishable the chylous chyliform and pseudochylous

1 Chylous fluid has a milky appearance does not coagulate does not undergo putrefaction and contains fat globules in a state of fine division Often it is associated with chylous ascites The condition originates from a rupture of the thoracic duct or from obstruction of the thoracic or smaller lymphatic ducts as a result of the pressure of tumors in the thorax Other etiological factors are thrombosis of the left subclavian vein and the occlusion of the lymphatics by trichinæ

2 The chyliform effusion has an appearance much like that of the chylous type but contains a higher percentage of fat and the globules are smaller (Norris and Landis[53]) Pus and enthothelial cells in the process of fatty degeneration are present in the fluid The chyliform effusion most often is associated with new growths and tuberculosis Clinically the chronicity of the condition is remarkable

3 The pseudochylous type is a sero chylous fluid less consistent than the preceding forms There are no fat globules to be seen under the microscope The opacity may be due to different substances Wallis and Scholberg[54] describe a lecithin globulin the removal of which renders the fluid clear West[55] attributed the milky appearance in his case to calcium phosphate Blankenhorn[56] found in a careful chemical study of five cases that the turbidity was due to very finely emulsified fat He believe the term pseudochylous misleading

Treatment follows the general indications of all pleural effusions Only temporary and symptomatic relief, however, can be expected from drainage

Pneumothorax from wounds of the chest has a symptomatology depending upon the size of the opening and whether it can be closed. Free admission of air not only brings about collapse of the lung on the affected side but by pressure on the mediastinum greatly embarrasses the opposite lung. Extreme dyspnea and circulatory failure may occur in the large or persistent openings.

Signs of Pneumothorax

The affected side of the chest is larger than the normal and less mobile. The expiratory excursion is slight in comparison with the exaggerated movements of the other side. Litten's shadow is absent. Displacement of the heart takes place but the apex impulse is difficult to see or is not visible because the air on one side and the compensatory expansion of lung on the other overlie the organ. The tactile fremitus is diminished or altogether absent. The lower edge of the liver displaced downward can be felt in right sided pneumothorax. Very rarely the spleen may be palpable with left sided pneumothorax.

The percussion note is loud and deep toned. The sound varies according to the state of tension of the gas. When under much tension the note is high pitched like the Skodaic resonance or is even dull; when under low tension the note is tympanitic like that elicited over the intestines. As the fluid accumulates dullness appears below and tympany above. The level of fluid is a horizontal line unlike the curved line of ordinary effusion. The level shifts as the position of the chest changes. A peculiar cracked pot resonance (Wintrich's sign) may be elicited if there is a communication between the pleural cavity and a bronchus.

As a rule the respiratory murmur is faint or absent. At times distant amphoric breathing can be heard. Râles high pitched and clear are audible over the area of the collapsed lung. One of the characteristic signs of pneumothorax is the "metallic tinkle" that is sometimes produced by coughing or deep breathing. The voice sounds may be muffled and distant or amphoric in quality. The succussion sound first described by Hippocrates is pathognomonic of air combined with fluid. To elicit this sign the patient is given a quick shake while the ear is applied to the chest. A splashing sound is heard distinctly and may be audible to the patient himself. The coin sound is produced by tapping a coin laid flat on the chest with another coin or piece of metal while the clinician listens over the different areas of the chest. By careful examination this phenomenon can be observed in the great majority of cases of pneumothorax.

empyema Tuberculosis outranks all other diseases combined as an etiological factor The weakening of the alveolar walls may lead to rupture during a coughing spell in chronic emphysema or in the acute emphysema of whooping cough In all these diseases cough by its sudden violent increase of intrapulmonary pressure may be the exciting cause of perforation Finally there is a type of spontaneous pneumothorax occurring in apparently healthy individuals due to the rupture of a bleb or a vesicle

An open pneumothorax permits the air to enter and escape alternately with inspiration and expiration through the perforation A closed pneumothorax is one in which the perforation becomes sealed after the first escape of air A valvular pneumothorax is one in which air enters the cavity during inspiration but cannot escape during expiration Perforation is found post mortem most frequently in the upper lobe in the space bounded by the second and fifth ribs and laterally by the axillary and mammary lines

A fistulous communication with the gastrointestinal canal occasionally is a cause of pneumothorax Carcinoma of the esophagus or stomach may initiate a fistulous opening into the pleural cavity with escape of gas A subphrenic abscess occasionally perforates the diaphragm and produces empyema which in turn finds an outlet through the lung thus permitting the entrance of air

Gas formation from anaerobic bacteria is seen exceptionally in the putrefactive empyema of shell wounds or in non traumatic infections

Symptoms of Pneumothorax

In a typical case of spontaneous pneumothorax occurring in phthisis during a coughing paroxysm the patient complains of a sharp stabbing pain in the chest the evidence of a localized pleurisy Dyspnea may be intense to the point of suffocation The pulse is rapid the skin is wet with profuse perspiration The picture is that of profound shock Death or recovery ensues depending on whether the perforation remains open or closes as the lung retracts The valvular perforation tends to augment constantly the pneumothorax during inspiration without allowing the escape of air during expiration Under favorable circumstances the degree of compression becomes stationary and little by little absorption brings gradual relief

A similar group of cases is characterized by a slow insidious onset and the recognition of the pneumothorax is first by examination of the chest or by the x ray Pain may be absent in these patients and the dyspnea is not conspicuous

Treatment of Pneumothorax

For the state of shock induced by the sudden rupture of the lung a hypodermic injection of morphin is indicated This alleviates the dyspnea and lessens the cough Thoracentesis is not a safe procedure as it is in simple pleuritic exudates and should be employed only after mature consideration The pressure of the intrapleural air collapses the lung and is itself the best means of closing the perforation Aspiration of the air tends to reopen the wound and aggravate the condition If asphyxia develops aspiration of a small portion of the air may be necessary although there is no certainty of giving relief

In seropneumothorax accompanying pulmonary tuberculosis the chances of recovery are better if there is no surgical interference The presence of pus with air must be treated along the same lines as simple empyema namely free drainage by incision The certainty of progressive sepsis in these cases outweighs the danger of expanding the wounded lung Likewise a putrid exudate with gas allows no alternative to thoracotomy The same principles are followed in the treatment of pneumothorax from chest injuries It is not necessary to remove the gas unless an extensive hemothorax or empyema render free drainage imperative

Gaping chest wounds should be closed as soon as possible Graham and Bell have shown that asphyxia occurs when the proportion of air in the pleural cavity exceeds a certain ratio to the amount of air entering the lungs Conditions tending to limit the entrance of air into the lung such as pneumonia phthisis and collapse of lung tissue enhance the danger of admitting air freely into the pleural cavity Hence in open chest injuries involving the lung every effort is made by the surgeon to convert the open pneumothorax into a closed pneumothorax

Spontaneous Pneumothorax in the Apparently Healthy

Although it has been appreciated for a long time that certain cases of spontaneous pneumothorax in apparently healthy individuals have a good prognosis it has been pointed out only recently that they represent a distinct disease entity both etiologically and clinically This condition is by no means rare

In these cases the pneumothorax is caused by the rupture of a bleb or vesicle frequently solitary which is not associated with emphysema or with active tuberculosis Usually the connection between the bleb and the bronchiole is such that it acts as a one way valve allowing air to enter the bleb only Apparently some of the blebs arise in the base of an

Diagnosis of Pneumothorax

The onset, history and physical findings generally are adequate to make the diagnosis Distention of the stomach with gas and liquids sometimes is mistaken for a left sided pneumothorax as it presses on the diaphragm and gives a tympanitic percussion note over the lower thorax This condition also gives rise to the succussion splash the metallic tinkle and rarely to the coin sound The history of the patient and the x ray will clear up a doubtful case A large tuberculous cavity of the lung may present amphoric breathing tympany and the metallic tinkle but seldom the coin sound and never the succussion splash With a cavity there is no bulging of the interspaces and no displacement of the thoracic viscera

Emphysema by reason of a tympanitic note and faint breathing has been confused with pneumothorax Emphysema generally is bilateral and not associated with fluid in the chest A pleuritic effusion may compress the lung above the fluid level so that the hyperresonant note closely simulates the tympany of pneumothorax

Subphrenic gas arising from perforation of the stomach may closely resemble pneumothorax The x ray will define closely the outline of the diaphragm and show the gas below The diaphragm in a case under our observation was forced three or four inches above the normal position

Diaphragmatic hernia in which the gas filled intestine or stomach protrudes into the thorax is very difficult to distinguish from true pneumothorax The diagnosis may be made by hearing borborygmus or more certainly by the x ray picture

Prognosis

The mortality of all cases of spontaneous pneumothorax is said to be about seventy per cent when associated with diseased lungs In the form of spontaneous pneumothorax described in the next section it is almost nil There is practically no danger from partial pneumothorax resulting from accidental admission of air during thoracentesis The outlook is favorable in the pneumothorax complicating emphysema and whooping cough Following empyema the prognosis is not so good Cases associated with tuberculosis abscess and gangrene rarely recover Pneumothorax resulting from chest injuries always is a serious menace to life According to Duval[57] fifty per cent of patients with lung wounds die within the first day as a consequence of pneumothorax and hemorrhage The mortality in gaping wounds is nearly twice as high as in closed wounds since the pneumothorax is greater and infection more frequent

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old scar for others no explanation is available That active tuberculosis is not an etiological agent has been definitely demonstrated by Kjaergaard[58] Out of 49 cases carefully followed only one developed pulmonary tuberculosis At autopsy this case showed tuberculosis on one side and a vesicle on the other side showing a complete lack of relationship

Clinically these cases can be recognized by the fact that they occur in otherwise healthy individuals without evidence of tuberculosis Usually there is no precipitating cause although occasionally a history of strenuous exertion straining or coughing is obtained The symptoms and signs of the pneumothorax are dependent on the rapidity and amount of air that escapes More than a small amount of fluid rarely collects and temperature usually is absent except for a very slight amount during the first few days

The prognosis is nearly always entirely good only 6 out of about 200 cases reported in the literature having been fatal The dangerous complications are tension pneumothorax bilateral spontaneous pneumothorax and hemopneumothorax Recurrences are common occurring in about twenty per cent of cases and usually during the first year In cases with only a small amount of air recovery is complete in one to two weeks In cases with complete collapse of the corresponding lung the air usually is reabsorbed in one to three months Occasionally reabsorption fails to occur for years

The treatment should be expectant and symptomatic with emphasis on preventing cough or constipation with their resulting strain on the lungs Bed rest is desirable until the air is absorbed (The Editor s experience is that they do as well if not better when ambulatory unless they easily become dyspneic) Heavy exertion should be prohibited for one year because of the danger of recurrences

Under certain circumstances more active therapy is imperative In *bilateral pneumothorax* and *tension pneumothorax* thoracentesis with removal of air is life saving and should be performed if there is the slightest suspicion of either of these conditions

Removal of air can be performed also in cases that fail to reabsorb rapidly It is desirable to wait for at least two weeks before such attempts are made so as to allow healing of the lung surface In some of the chronic or repeatedly recurrent cases an adhesive pleuritis can be induced by injecting various irritating substances into the pleural cavity

Hemopneumothorax as the result of hemorrhage from the torn bleb is a serious complication for two reasons (1) the symptoms frequently are those of an acute abdominal lesion so that the diagnosis is confused

and (2) there is danger of a fatal hemorrhage Thoracentesis frequently is advisable here as well

It is important in this condition to realize that unless there are specific signs of tuberculosis it is not necessary to institute sanatorium care Kjaergaard has shown with reasonable certainty that a spontaneous pneumothorax falling within this group need not be treated as an indication of tuberculosis as has often been done in the past

Artificial Therapeutic Pneumothorax

Induced pneumothorax generally is considered now to be a most valuable method in the treatment of pulmonary tuberculosis It has long been recognized that a pleural effusion or a spontaneous pneumothorax may exert a favorable influence on a phthisical lung Artificial pneumothorax not only serves to immobilize and put at rest the affected organ but it also tends to obliterate cavities Due to the diminished circulation of blood and lymph fibrosis and healing are stimulated Symptomatically fever and toxemia are diminished and expectoration decreased Hemorrhage frequently is stopped Artificial pneumothorax may be used in selected cases of bilateral pulmonary tuberculosis as well as in unilateral involvement The presence of extensive adhesions makes the introduction of air into the pleural cavity difficult or impossible and prevents collapse of the lung Cases of active tuberculosis where bed rest alone fails to halt the progress of the disease should in general be considered as candidates for this form of treatment For further details the reader is referred to the extensive literature on the subject[58, 59] and to the section on tuberculosis

Artificial pneumothorax has been used also in an effort to collapse bronchiectatic cavities and lung abscesses[60] In these conditions usually it is not very successful because the wall of the cavities are too rigid and because of the presence of adhesions Recently there has been a revival of interest in the use of this treatment for lobar pneumonia[61] As yet too few cases have been treated to justify an evaluation of the results

NEOPLASMS OF THE PLEURA

Neoplasms of the pleura nearly always are secondary to tumors arising elsewhere in the body Primary tumors of the pleura although rare do occur Attempts should be made to recognize them because of the possibility of successful treatment offered by modern thoracic surgery Klemperer and Rabin[1] recently have classified the primary neoplasm

of the pleura into the localized and diffuse forms The former arise from the subendothelial tissues of both the parietal and visceral pleura and include all varieties of malignant and benign tumors Thus we find fibromas chondromas leiomyomas angiomas lipomas and sarcomas The so called giant sarcomas and lipomas arising from the visceral sub pleural tissue are noteworthy as being non malignant and yet because of their size usually they cause death The diffuse pleural neoplasms are probably always malignant and have been variously called endotheliomas sarcomas and mesotheliomas

Symptoms and Signs of Neoplasm of the Pleura

Benign tumors seldom give rise to symptoms other than those caused by pressure Where the tumor is very large the pressure may be sufficient to obstruct the circulation and cause death[3, 61]

Malignant growths of the pleura are characterized by pain in the chest which is aggravated by respiratory movements There may be a cough but it is not always present Dyspnea develops in proportion to the amount of fluid in the chest and to the compression of the lung and the heart Fever is exceptional

The physical signs usually are those of a pleural exudate Examination of the fluid shows the presence of blood which increases with each successive tapping it may become coffee colored Under the microscope endothelial cells are found in abundance with comparatively few leucocytes The fluid reaccumulates rapidly and the patient becomes anemic and cachectic

Diagnosis

In most instances of malignant tumors of the pleura the initial diagnosis is of a pleural effusion When the exudate is withdrawn and found to be hemorrhagic the suspicion is aroused of tuberculosis or neoplasm Histological section of a supraclavicular lymph gland may permit a differentiation Absence of fever of advanced tuberculous lesions in the lungs and of tubercle bacilli in the sputum furnish evidences against tuberculosis On the other hand a history of a preceding cancer of the breast of the gastrointestinal tract or of the prostate may weigh in favor of a secondary neoplasm

The x ray may aid in determining the nature of the tumor especially as to its location and whether it is localized or diffuse Frequently the production of a small pneumothorax is very helpful Lipiodol also can be

used occasionally to advantage Biopsy either by endoscopy or by direct surgical approach is of course desirable especially if the tumor appears operable

Prognosis

The duration of life in malignant pleural tumors varies from three to eighteen months The end often is hastened by some intercurrent infection such as bronchopneumonia Benign pleural tumors are dangerous only when they are of large size It is desirable to observe small tumors at frequent intervals in order to determine whether or not they are growing rapidly

Treatment

If the diagnosis of a benign primary pleural tumor can be made and if it is large enough to produce serious symptoms or if it is growing rapidly surgery should be considered Modern surgical methods make it possible to remove many of these growths with comparative safety

In either primary or secondary malignant tumors the administration of morphin is advisable to control pain Tapping the chest for withdrawal of fluid gives temporary relief in some cases Occasionally however drainage of the fluid augments the pain while it mitigates the dyspnea In a case of the author s the pain following the tapping was relieved by injecting 100 to 200 c c of sterile air after withdrawing 500 to 1 000 c c of fluid

RARE DISEASES OF THE PLEURA

Echinococcus Cysts of the Pleura

Echinococcus is the most common of the animal parasites to invade the pleura The ovum of tenia echinococcus has its habitat in the intestine of the dog and is expelled in the feces When ingested by man through the medium of contaminated water or hands the ovum reaches the stomach and loses its outer covering Thereupon it penetrates the stomach wall and in the majority of cases reaches the liver Frequently the ovum gains access to the pleura and lung presumably by way of the diaphragm The relative frequency of invasion of the right lower lobe suggests the likelihood of a route from liver to the pleural cavity

Once lodged in the pleural membrane or lung the ovum undergoes

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CHAPTER VI

DISEASES OF THE MEDIASTINUM

By JAMES S. McLESTER

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General Considerations

The mediastinum is of interest because of the important structures it contains. This interest is increased by reason of the inaccessibility of these structures and the consequent difficulties which surround all operative attempts within this space. At the same time it is not customary in writing of the mediastinum to consider those diseases to which all these very structures are subject, such, for instance, as aortic aneurysm or myocardial disease, since these are dealt with more appropriately elsewhere, but rather to discuss those pathological processes which involve chiefly the lymphatic tissues and the framework of the mediastinum. Such processes may originate locally, may appear as metastatic invaders, or may come by extension from surrounding structures. The patient is usually apprised of their presence by pressure effects.

Anatomically the interpleural space known as the mediastinum is limited anteriorly by the sternum and posteriorly by the spine. It is divided into a superior and an inferior mediastinum by the upper border of the pericardium, and this latter space in turn into an anterior, a middle and a posterior mediastinum, with the pericardium and its contained heart occupying the middle space.

Viewed from a clinical standpoint this space is best considered as a whole, or perhaps roughly divided into anterior and posterior parts. The structures contained in the mediastinum are the heart enclosed in the pericardium, the aorta with its great branches, the superior vena cava with its tributaries, the inferior vena cava, the pulmonary artery and veins, the thoracic duct, the vagus, cardiac, phrenic and left recurrent laryngeal nerves, the esophagus, the trachea and bronchi, the remains of the thymus gland, and numerous lymph nodes.

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In their gross structure the lymphosarcomas are more lobulated than the spindle cell variety They tend to grow in the direction of least resistance and to envelop opposing structures rather than to push them aside hence with lymphosarcomas we may expect fewer pressure symptoms

Sarcoma of the mediastinum may occur at any age and between ten and sixty its distribution is fairly even

Endothelioma of the mediastinum is occasionally encountered These tumors may arise in the lymph nodes of the mediastinum or may come by extension from the pleural endothelium

Primary Carcinoma of the mediastinum contrary to the belief of earlier writers is extremely rare Hare reported 134 cases of cancer and only 98 of sarcoma in his collection of 5[illegible]0 cases of mediastinal disease but Christian[2] very aptly calls attention to the fact that Hare accepted without question the reports of the earlier authors many of whom wrote at a time when in the light of our present knowledge their diagnosis and terminology must have been faulty He quotes Lohrish as being able to find but two instances of true mediastinal carcinoma reported in the years 1896 to 1901 and adds another reported in 1906 These tumors can originate in the mucous membrane of the esophagus trachea bronchi thymus or misplaced thyroid sometimes from fetal inclusions

Carcinoma elsewhere in the body differs from sarcoma in that the former is accompanied with relative frequency by metastasis in the mediastinum Such secondary growths may have their origin anywhere in the body but most often they come from the mammary gland or the lung and locate first in the lymph nodes at the hilus of the lung Moderate enlargement of the posterior mediastinal lymph nodes discovered in the radiogram is occasionally seen as the first intimation of an esophageal cancer

The Thymus which ordinarily atrophies before the age of carcinoma development sometimes gives rise to a malignant tumor of homogeneous structure whose nature is uncertain and which consists of certain round cells suggesting the parenchyma cells of the thymus This tumor should properly be reckoned among the sarcomas rather than among the carcinomas

A misplaced *Thyroid Gland* situated in the thorax between the sternum and the trachea or an accessory thyroid gland in this location may give rise to a tumor of sufficient size and rapidity of growth to embarrass the patient and produce pressure symptoms Such a tumor may be a simple adenoma or it may assume the malignant characteristics of a sarcoma or carcinoma

Benign Tumors of the mediastinum are rare and since they grow slowly and do not form metastases they seldom produce symptoms Most often they represent merely a chance find at autopsy In this group belong the

The functions of the mediastinum have been defined as threefold[1] (1) it forms a septum between the two lungs making each more or less independent of the other as regards intrathoracic pressure (2) it lodges certain important channels of communication and (3) it serves as a lymphatic area which contains many nodes and toward which all lymph channels lead

Classification —For our present purposes the following classification of diseases of the mediastinum seems best

I *Tumors of the Mediastinum*
- A Solid Tumors
  1 Sarcoma and Lymphosarcoma
  Carcinoma
  3 Endothelioma
  4 Thyroid Tumors
  5 Fibroma Lipoma Myoma and Chondroma
  6 Enlarged Lymph Nodes
- B Cysts
  1 Simple
  Echinococcus
  3 Dermoid

II *Inflammation of the Mediastinum*
- 1 Lymphadenitis
- Acute Mediastinitis
- 3 Chronic Mediastinitis

III *Other Diseases of the Mediastinum*
- 1 Emphysema
- 2 Hemorrhage
- 3 Hernia

Solid Tumors of Mediastinum

Since the symptoms and signs of a mediastinal tumor are dependent upon its size location and consequent pressure effects rather than upon its nature and since at the bedside it is frequently impossible to determine the pathological character of such a growth the following discussion will consider all solid tumors as a whole

Sarcoma is the most common mediastinal tumor It may be of the spindle cell variety though rarely a giant cell or melanotic sarcoma is encountered or it may belong to that group of tumors of varying cell type and behavior to which the name lymphosarcoma has been given Among these last should be included the round cell sarcoma the lymphoma, the lymphocytoma and such borderline tumors as the so called lymphosarcoma of Kundrat or the leucosarcoma of Sternberg The thymus tumor to which allusion is made below should also be grouped with the sarcomas

The growth usually arises from the mediastinal connective tissues the lymph nodes or the thymus rarely from the esophagus the air passages or the pericardium or it may come as an extension from the lungs or pleura Sarcoma of the mediastinum is seldom metastatic in origin

the most graphic physical signs (2) those of the posterior mediastinum which by pressure upon the esophagus trachea and intercostal nerves induce distressing subjective symptoms and (3) those which extend from pleura or lung with both physical signs and symptoms in like proportions

The onset of symptoms is most often gradual and slow It sometimes happens that an individual harbors a mediastinal tumor for years with slight discomfort yet in rare instances we may see him experience the fulminant development of all symptoms with a rapidly fatal ending

Dyspnea cough and pain are the most frequent symptoms while circulatory disturbances offer the most constant physical signs The patient usually complains first of shortness of breath on exertion of cough or perhaps of both He tells of a gradually increasing dyspnea which at first may be paroxysmal in character with long periods of complete relief This may be the only symptom for months and it must be borne in mind always that respiratory distress which cannot be explained by disease of the heart or lungs should suggest mediastinal tumor Gradually the dyspnea becomes more oppressive and less dependent upon exertion or emotion as the tumor with its consequent pressure increases in size The continuous distress and the inability to sleep in a recumbent posture leads to exhaustion and finally only too frequently the dyspnea ends in suffocation

Cough is a frequent symptom and is often paroxysmal in character It may be wheezy and perhaps accompanied by stridor A peculiarly characteristic brassy cough accompanies hypertrophy of the tracheobronchial and peribronchial lymph nodes particularly in children

The sputum is variable being usually the mucous expectoration of bronchial irritation At times it is bloody or as evidence of a secondary infection of the air passages it may be purulent Its bloody character with the fever which sometimes accompanies mediastinal tumors has led to a mistaken diagnosis of pulmonary tuberculosis

At first the patient may complain of a sense of constriction or oppression in the chest Later this becomes a real pain which is usually substernal and varies greatly in intensity and constancy Though present in the later stages with great frequency at times pain may be absent throughout the entire course of the disease Dysphagia or esophageal pain is an occasional complaint especially when the pressure of the tumor is exerted chiefly in the posterior mediastinum

Vagus irritation may lead to asthma like attacks or other respiratory disturbances to cough to spasm of the glottis to bradycardia or if the nerve is paralyzed to tachycardia Paralysis of the recurrent laryngeal nerve occurs occasionally though less often here than in aneurysm Even in the absence of hoarseness or other laryngeal symptoms vocal cord paralysis should be sought for with the laryngoscope Irritation or paralysis of

fibromas lipomas myomas chondromas and osteochondromas An exception to this general statement is the dermoid cyst which will be discussed later

Enlarged Mediastinal Lymph Nodes, whether simple or tuberculous deserve mention here because they sometimes form tumor masses of great size and produce pressure symptoms identical with those of other tumors Inflammatory reaction in these tissues will be reserved for discussion with mediastinitis

Pigmentation and sclerosis as a part of the process known as anthracosis is frequent in those who habitually breathe air laden with coal dust and the mediastinal glands of stone cutters are said to show a similar sclerosis The writer has been particularly impressed by the dark color of the bronchial lymph nodes of individuals who have lived long in the Birmingham Alabama district

Simple hyperplasia of these nodes even without infection it is said may take place as the result of any infection whose products drain into the mediastinal lymph spaces Usually such masses which are most often peribronchial are insufficient in size to produce discomfort but occasionally as the result of a chronic or frequently recurring bronchitis in children the nodes attain sufficient size to call forth definite pressure symptoms

In Hodgkin s Disease and in leukemia similar enlargement of the mediastinal lymph nodes is encountered and in each the masses may attain sufficient size to produce distressing symptoms Both of these diseases are accompanied by glandular enlargement elsewhere and before mediastinal pressure symptoms are experienced hypertrophied nodes in the neck and other parts of the body usually may be felt

Such masses of enlarged lymph nodes are heterogeneous in structure consisting of a conglomerate mixture of lymphoid and connective tissues As would be expected they are irregular and nodular in outline and frequently no definite boundary line can be seen in the radiogram between the tumor mass and the lung area

Symptoms of Mediastinal Tumors

The symptoms of mediastinal tumors confined as these tumors are in a definitely limited space which houses a number of vitally important structures are dependent whatever the nature of the tumor upon the pressure which is exerted upon these structures Every degree of pressure constriction and displacement is encountered in such tumors and the widest variation in intensity and combination of symptoms

Three clinical types can be roughly recognized (1) tumors of the anterior mediastinum which by obstruction of the venous circulation produce

ratory sounds are well transmitted through such a lung Pleural effusion is present very often and may be so extensive as to obscure the tumor

Signs of venous obstruction do not ordinarily appear until the superior vena cava has been constricted to about three fifths its original diameter[3] These signs are dilation of the veins cyanosis and edema At a certain stage they may be striking later to disappear as the collateral circulation becomes well established

Usually the veins in the neck are the first to dilate standing out as prominent cords Others over the neck and chest then become involved until finally an elaborate network of prominent outstanding anastamosing veins has appeared to take up the collateral circulation In typical instances the venous dilatation is general over the upper half of the body or depending upon the location of the pressure within the chest it may be localized Cases of one sided dilatation and edema have been reported The course and distribution of these veins is more particularly described in the discussion of chronic mediastinitis Accompanying sometimes preceding these startling vascular changes is a striking subcutaneous edema first of the neck and then of the arms and chest Rarely it may be more definitely localized

Cyanosis develops simultaneously with the vascular change or may appear independently A blueness of the lip and a generally increasing duskiness of the face is often an early objective sign This may of course be produced merely by respiratory distress before marked obstruction of the veins has occurred

Polycythemia of moderate grade is a concomitant of the venous obstruction The number of erythrocytes and the percentage of hemoglobin are usually high and especially so during the paroxysms of increased dyspnea and cyanosis when values as high as nine million and one hundred and forty four per cent respectively have been reported A difference in the counts made from the ear and from the toe is sometimes noted in such patient Dilatation of the retinal veins and edema of the optic disk is a frequent result of such circulatory disturbances

Radiology gives valuable help in the recognition and identification of these tumors and permits a view of mediastinal masses before symptoms or pressure signs appear Every person with a malignant tumor wherever located might well be given a radiologic examination of the mediastinum before operation to discover any possible mediastinal metastasis whose presence would influence operative treatment Whenever possible both radioscopy and radiography should be used If one must choose the former gives perhaps more valuable information since pulsation and movement can be observed yet the latter brings out more closely the finer details of structure and permit more precise study

the vagus from mediastinal pressure is said also to lead to such abdominal symptoms as nausea and those of gastric hyperacidity as well as to intestinal disorders Pressure upon the sympathetic nerves may produce pupillary dilatation exophthalmos or one sided hyperidrosis

Involvement of the phrenic nerve sometimes leads to unilateral paralysis of the diaphragm but in the same connection it must be borne in mind that a very similar phenomenon may be produced by occlusion of a bronchus Irritation of the peripheral nerves particularly the rami communicantes may produce pain at a point distant from the source of the pressure Such a pain has been experienced in the ulnar nerve The writer recalls a patient in whom for a long period the only symptom of a malignant mediastinal tumor was a most distressing intercostal pain

Cachexia and fever are occasionally seen more often in tumors of the posterior mediastinum Pressure upon the thoracic duct is said to produce *sudden wasting occasionally chylous ascites has this origin Headache* dizziness and disturbances in vision are occasional symptoms

The most marked symptoms as well as the most graphic signs are produced by pressure upon the inferior vena cava the result of which will be discussed below The aorta because of the stronger arterial wall is seldom constricted although a pressure necrosis of this vessel with fatal hemorrhage has occurred

Physical Signs of Mediastinal Tumor

A local bulging of the chest is frequently seen or perhaps a fullness of the intercostal spaces and so important is this that the slightest asymmetry should always receive attention Localized edema and injected veins over the tumor area are sometimes observed Sarcoma of the anterior mediastinum tends to grow forward pushing in front of it the sternum and ribs rarely eroding them Enlarged lymph nodes in the neck are frequent and occasionally the tumor mass may be felt above the suprasternal notch Deviation of the trachea especially in intrathoracic tumors of the thyroid gland may indicate mediastinal pressure Localized pulsation of the chest wall not expansile in character is frequently felt

Dullness or flatness on percussion *over the tumor or perhaps* merely an extension of the normal cardiac area of impaired resonance is often noted Posteriorly under normal conditions the percussion note which is dull over the last cervical vertebra gradually becomes more resonant from the first *to the fifth dorsal vertebra and is clear but not tympanitic from the sixth* to the ninth dorsal vertebra Tumors of the mediastinum are said to modify this clear note Diminished or absent tactile fremitus and absence of the respiratory murmur may be noted over those areas where atelectasis of the *lung has followed pressure upon a large bronchus* yet occasionally *the respi*

indicate The presence in the former of an expansile pulsation is the classical differential sign but it must be borne in mind that solid tumors frequently transmit a pulsation which may be deceptive in character and that instances have been reported where an aortic aneurysm because of a thick wall of fibrin within its sac failed to show the typical pulsation



Fig —(*Case 1*) Tumor April 1914 practically cleared up under radium therapy (*Courtesy of Doctor C F Burnham*)

Aneurysms best seen in the left posterior oblique position are sharply outlined but unfortunately malignant tumors as a rule show the same sharp detail If beside the shadow of a mass the arch of the aorta can be recognized in normal position this speaks against aneurysm although the converse is not true since a large tumor can greatly displace a normal aorta

Certain general facts are of value in the differential diagnosis of tumors of the mediastinum Sarcoma which is by far the most frequent is usually seen in the anterior mediastinum while of the tumors of the posterior

The mediastinum should be viewed from every direction antero posteriorly laterally and obliquely The right anterior oblique direction permits a good view of the clear space between the heart and the spine The left posterior oblique direction gives a less distinct view of the same area Stereoscopy is useful in giving better orientation and resort to



Fig 1 —(*Case 1*) Large lymphosarcoma of mediastinum which bulged above the clavicle exteriorly June 4 1913 (*Courtesy of Doctor C F Burnham*)

teleroentgenography may be had as a method of recording the progress of a growth

Differential Diagnosis

It is relatively easy to determine the presence of a mass in the mediastinum and by its pressure symptoms we can usually tell something of its size and location but the nature of the mass is only too often a matter of conjecture

To distinguish between aortic aneurysm and a growth of the mediastinum is not always as easy as a statement of the differential signs would

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Fig 2 – (*Case 1*) Tumor April 1917 practically cleared up under radium therapy (*Courtesy of Doctor C F Burnham*)

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mediastinum particularly in children tuberculous adenitis is to be considered The character of the sputum will sometimes disclose a dermoid cyst The Wassermann reaction may reveal the nature of gummatous growths and is also one link in the evidence for aneurysm



FIG 3 —(*Case 2*) Deep seated media tinal tumor which caused difficulty in deglutition November 7 1914 (*Courtesy of Docto C F Burnham*)

In distinguishing between a true mediastinal tumor and those of the lung it is a general rule with many exceptions that the former show sharp outlines in the radiogram while the latter reach out into the lung with irregular faint shadows

A thorough clinical study of the patient from every standpoint is essential, for it often happens that findings outside the mediastinum will clear the diagnosis such for instance as a malignant tumor elsewhere the blood changes of leukemia or evidence of Hodgkin s disease or generalized tuberculosis

Prognosis

Regarding prognosis the malignancy of a mediastinal tumor depends not so much upon its pathologic structure as upon its location and the rapidity of development. Depending upon these factors it may run a

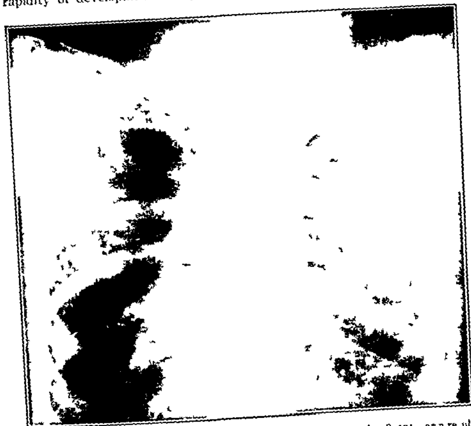


Fig 4 —(*Case* [illegible]) Almost complete disappearance of tumor November 8 191[illegible] as a result of about six months radium treatment apparently complete recovery of patient (*Courtesy of Doctor* A F *Burnham*)

rapidly fatal course within a few months may continue for two three or four years or may pursue a relatively unobtrusive course for many years

Treatment

Concerning treatment malignant tumors are best treated with radium and when this is not available X rays should be tried. Burnham[4] has recently reported some excellent results (see Figs 1 [illegible] 3 and 4) from the use of radium in which he states that at least one gram of radium is necessary

and that lead filters should be used to protect the skin Von Bergmann advises also the energetic use of arsenic though with what reason it is difficult to see

Temporary amelioration of symptoms has been achieved by the surgical device of splitting the sternum and thus relieving intrathoracic pressure Enlarged glands of the posterior mediastinum which are producing pressure symptoms can sometimes be satisfactorily reached by surgical measures through the back Gummata are amenable to energetic antiluetic treatment

Cysts of Mediastinum

Cysts of the mediastinum may be simple echinococcus or dermoid and among the last named we include the teratomas

Simple Cysts of the mediastinum which are small and usually lined by a single layer of ciliated epithelium are rare Most of those reported have been in the neighborhood of the tracheal bifurcation *Echinococcus Cysts* are also rare and grow slowly producing symptoms only when they have reached great size

Dermoid Cysts and *Teratomas* of the mediastinum also are uncommon Christian[5] in 1901 collected forty cases and in 1905 Morris[6] in an excellent summary of the literature of that time brought the total number to fifty seven Hertzler[7] in 1916 brings the number to seventy three since which time I have been able to find two additional cases[8, 9] thus giving a total to date of seventy five

These growths vary in complexity from the simple cyst lined by squamous epithelium to the most complex cystic tumors such as the one recently described by Lindstedt[8] as an adeno chondro myxocarcino sarcoma Christian[10] classifies these cysts as (1) dermoid cysts of simple structure and ectodermal origin (2) teratomas of great complexity with rudimentary organs derived from all three germ layers and (3) tumors of either of the foregoing classes which are malignant in some part of their structure and form metastases For the present purposes of clinical discussion it is best to consider all three classes as one

These cysts represent fetal inclusions being formed in the closure of the fetal clefts or by infolding of the embryonic glandular structures Sex has no bearing on their frequency Although they may appear at any age they are most often seen in the third decade

Dermoid cysts may be found anywhere in the mediastinum but their most frequent location is in the anterior part of the upper mediastinum They grow variously in every direction pushing the chest wall forward extending above the clavicle into the neck or reaching laterally into the area ordinarily occupied by the lungs and not infrequently they press

backward upon the great vessels They seem to exert an irritating influence upon the surrounding tissues forming dense and extensive adhesions to neighboring structures It has been suggested that the tumor content at a certain stage undergoes a change similar to that seen in wens which makes it more irritating and leads to an inflammation of the cyst wall with adhesions to surrounding tissues These adhesions are usually to the pleura or pericardium seldom to the esophagus or trachea and because of their density removal of the growth is quite a hazardous procedure In size the cyst may be of any conceivable dimension and may contain quantities of fluid

The Symptoms of Dermoid Cysts of the Mediastinum do not ordinarily present themselves until puberty or soon thereafter the cyst remaining latent during early life Pain usually substernal is frequent and dyspnea is often distressing The dyspnea in this as in other diseases of the mediastinum is most often paroxysmal in character and in the early stage is dependent upon exertion There may be long periods of remission but later in the progress of the growth dyspnea is the most constant symptom

Cough is frequent The sputum which is usually profuse may present no characteristic features being merely the result of chronic irritation of the bronchial mucous membrane At other times the cyst through pressure necrosis bursts into a bronchus and the expectorated material contains hairs fat droplets cholesterin crystals and other bodies highly characteristic of such a growth Search should always be made for such substances where a dermoid cyst is suspected Frequently the sputum is blood tinged and there may be active or even profuse hemoptysis Sometimes bronchoscopy will tell the tale as in Hamman s* life long suffering with asthma in whom the opening of the cyst into a bronchus was discovered

Fever is a frequent symptom and always present when the cyst ruptures into a bronchus with resulting infection of its contents Pleural effusion is sometimes noted

The *Physical Signs* are variable There may be bulging of a part of the anterior chest wall and this may show fluctuation The chronicity of the process presenting such appearances often suggests the nature of the tumor but differentiation from an encapsulated empyema may be difficult Other physical signs of tumor such as dullness on percussion and absence of breath sounds will sometimes be found Radiograms are especially helpful and where teeth or bone are recognized in them as a part of the growth the diagnosis becomes certain

The *Prognosis* without operation is grave and not infrequently the cyst undergoes malignant change With operation the mortality is about thirty per cent Incision and drainage is the most frequent resort since often complete removal is impossible

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occurs in a variety of conditions and in pneumonia particularly is an extension of the inflammation on the mediastinum almost invariable In pericarditis and pleurisy and in septicemia the infection frequently reaches the mediastinal tissues

Abscess of the Mediastinum

Abscess of the mediastinum arises in the order of frequency by extension by metastasis or from trauma The suppurative process may extend from a retropharyngeal or a peritonsillar abscess (the most frequent source) a tuberculous vertebra or rib a caseating lymph node a ruptured pleural empyema or perhaps a perforating ulcer of esophagus or air passage The suppuration may be general with purulent infiltration of all the mediastinal tissues or it may lead to the formation of a circumscribed collection of pus

Metastatic abscesses were in the past relatively rare appearing occasionally in the course of septic processes or in certain other diseases such as typhoid fever but during 1917 and 1918 such abscesses were a frequent complication difficult of recognition of influenza pneumonia Thus mediastinal abscess takes its place in the history of this epidemic alongside empyema of the pleura and the pericardium At Camp Sheridan the writer was not infrequently surprised to find a mediastinal abscess in patients with pleural empyema who continued fever and other symptoms after drainage of the pleura had become a source of worry and perplexity

Mediastinal abscess following penetrating wound of the chest or fracture of the sternum is an occasional occurrence The mediastinal hemorrhage resulting from the trauma offers a fertile medium for the development of an abscess It is said that the latter injury is overlooked with surprising frequency Collections of pus in the posterior mediastinum of children are not infrequently seen as the accompaniment of caries of the spine or of a caseating tuberculous lymph node

The *Symptoms of Mediastinal Abscess* are frequently masked by the disease from which it has arisen Pain usually substernal but sometimes near the spine throbbing in character and intensified by pressure fever often septic in type evidences of pressure on the veins or air passages and edema of the chest wall are frequent symptoms Such abscesses are usually to be found just beneath the sternum or near the spine and their location may be indicated by impairment of the percussion note More precise information is to be had from a radiogram

An abscess of the mediastinum whether diffuse or circumscribed may rupture into the esophagus trachea or pleural cavity though occasionally it finds an outlet through the intercostal spaces or above the clavicle

Inflammation of Mediastinum

Inflammatory reaction in the mediastinal lymph nodes may assume the form of (1) simple hyperplasia with tumor formation (2) a more active process such as is seen in certain septic conditions and in miliary tuberculosis or finally (3) caseation The first of these was discussed with tumors of the mediastinum

These nodes become infected in many diseases especially in bronchitis and pneumonia Living organisms such as the streptococcus pneumococcus and the tubercle bacillus have been found in the tracheobronchial lymph nodes of presumably healthy individuals dying of accident[11] The milder forms of reaction seldom produce recognizable symptoms but occasionally an adenitis is of sufficient intensity to spread to the surrounding structures and thus give rise to a general mediastinitis or a resulting sclerotic process may produce a traction diverticulum of the esophagus trachea or bronchi

Tuberculosis of the Mediastinal Lymph Nodes is especially common in children forming in all likelihood the portal of entry for this infection to the lungs and it is thought that the tubercle bacillus reaches these glands through the naso pharyngeal mucosa and the cervical lymph nodes This infection may remain latent and local for years even indefinitely or when forced into view it may represent merely one phase of a generalized process

The peribronchial lymphadenitis of childhood is the most frequent form These nodes vary in size from the smallest tumors scarcely to be seen in the radiogram to large conglomerate masses with pronounced pressure symptoms Caseating tuberculous lymph nodes are a frequent source of mediastinal abscess

The symptoms produced by tuberculous nodes differ but little from those produced by other mediastinal tumors As a rule there are no symptoms but the resulting bronchial irritation sometimes produces a paroxysmal brassy cough resembling that of pertussis and a low grade fever difficult of explanation is a frequent accompaniment Larger masses may produce pain posteriorly in the subscapular region or anteriorly beneath the sternum

Occasionally the glandular masses are sufficiently large to alter the percussion note and respiratory murmur posteriorly near the spine or anteriorly over the sternum but most often the nodes are to be recognized only in the radiogram

The treatment is that of tuberculosis elsewhere unless caseation has produced an abscess requiring operation

Acute Mediastinitis

Acute mediastinitis may be serous fibrinous or purulent A certain amount of inflammatory reaction of these tissues frequently unrecognized

Cyanosis of the arms and chest ensues and the contrast in the appearance of the upper and lower halves of the body becomes striking. Headache and dizziness tend to become constant and epistaxis is frequent.

Still later when the collateral circulation has become well established the congestion and edema disappear and in their stead are seen widely dilated veins running down the face, neck, arms and upper chest. The blood of this network is carried to the inferior vena cava by two large trunks which join the cutaneous branches of the inferior epigastric and the long cutaneo thoracico epigastric veins. This anastamosis differs from that due to inferior vena cava obstruction, for in instances of the latter the dilated veins are usually upon the lateral part of the abdomen and empty into the axilla. It differs from portal obstruction in that with the last named the venous dilatation is most marked over the insertion of the diaphragm and the pit of the stomach and the collecting trunks empty into the medial and parasternal vein. The thoracic duct within the mediastinum may be involved by the connective tissue changes of the mediastinitis leading to chylous ascites.

An excellent example of the inferior mediastinitis with constriction of the inferior vena cava is seen in Pick's pericardial pseudo cirrhosis of the liver. This occurs usually in young individuals, rarely in the elderly, and may be distinguished from the true liver cirrhosis by the absence of any cause for such cirrhosis and by a history and physical signs suggesting pericarditis.

When the sclerotic process involves mainly the bronchi respiratory distress is most in evidence. Dyspnea is complained of with some cyanosis but no edema. There may be stridor and vocal symptoms referable to pressure upon the left recurrent laryngeal nerve.

The *Physical Signs of Chronic Mediastinitis* are variable. There may be a dull note on percussion over the sternum or posteriorly in the interscapular region. Siebert[15] has described a loud blowing continuous murmur independent of the cardiac cycle heard best close to the sternum in the second right interspace which is made louder by deep inspiration or by holding the breath. Howard[16] quotes the description by Ferez of a to and fro creaking friction rub heard over the manubrium sterni when the arms are moved up and down as in artificial respiration. He states that this rub was striking in his two cases and not found with anything like equal intensity in other diseases. Inspiratory intermission of the pulse or pulsus paradoxicus as it is called is frequently absent. Tracheal tug is seldom found but there is frequently seen a pulsation of the larynx and trachea synchronous with the heart beat to which the term pulsus transversalis has been given[18]. On the other hand complete immobility of the larynx in swallowing and talking is sometimes observed.

The prognosis is grave but not hopeless depending upon prompt recognition and surgical interference[1]

Chronic Mediastinitis

A number of pathological processes are grouped together under the term chronic mediastinitis The feature common to all is an intense thickening of the connective tissues of the mediastinum with ever increasing adhesion and eventual matting together of the mediastinal structures The causes are threefold[13] (1) syphilis which produces the most frequent and characteristic form with an infection that is often so mild in its early manifestations as to have escaped treatment (2) tuberculosis, usually of the lymph nodes sometimes of the bony structures and rarely of a diffuse interstitial form and (3) other infections either focal or general with or without pericarditis Among these last are included such focal infections as tonsillitis or oral sepsis and such general diseases as septicemia scarlet fever or measles The heart with its pericardium often has formed the starting point for this adhesive process giving rise to the familiar term indurative mediastino pericarditis

The sclerotic process is not always evenly distributed for syphilitic lesions frequently predominate in the superior and anterior mediastinum while tuberculosis shows a tendency to involve the lower and posterior half The location of the greatest activity determines the symptoms and upon this basis we recognize roughly four types resulting from (1) a general diffuse infiltration without predominance of any one group of symptoms (2) adhesions which involve and partially obstruct the superior vena cava with constant stasis the most common and characteristic form (3) constriction of the inferior vena cava with resulting liver cirrhosis a rare form (Pick[14]) and (4) involvement of the bronchi in the sclerotic process with resulting respiratory distress In addition there is a latent form difficult of recognition because of the paucity of symptoms

The *Symptoms of Chronic Mediastinitis* depend in large degree upon the nature of the mediastinitis and the region chiefly involved In the most common form with obstruction of the superior vena cava the onset is usually slow and progressive At first there is dyspnea especially on effort then paroxysms or precordial pain often intense and accompanied by tachycardia with a sense of precordial constriction cyanosis or giddiness on stooping over a constant symptom and headaches which are sometimes relieved by epistaxis

Later the changes in the patient s appearance are startling The cyanosis becomes permanent and edema occurs in the congested area The swollen bloated face is of a bluish red color the features are difficult of recognition and the prominent eyes seem to be starting from their sockets

TABLE I

DATA CONCERNING SIXTY CASES OF ACUTE AND CHRONIC MEDIASTINITIS ASSEMBLED BY KEEFER

	Total Cases	Recovery	Death
A Abscess of anterior mediastinum			
I Acute abscess depending on			
a Osteomyelitis of sternum	1		1
b Ulceration of larynx	4		4
c *Cellulitis of neck*	-		
d Infarct of lung	1		1
e Pneumococcic infection	1	1	
Total	9	3	6
II Chronic mediastinitis from			
a Syphilitic mediastinitis			
1 Tracheal stenosis thrombosis of left innominate and jugular vein	1	1	
2 Thrombosis of superior vena cava	1		1
3 Aneurysm of aorta thrombosis of left innominate vein	1		1
b Mediastinopericarditis			
1 Syphilis with aneurysm of aorta	1		1
2 Rheumatic heart disease with mitral stenosis	3		3
c. Cause undetermined		1	1
Total	9	2	7
B Abscess of posterior mediastinum			
I Acute abscess			
a Perforation of esophagus by			
1 Foreign body	9	3	6
2 Carcinoma of esophagus	7		7
3 Aneurysm of aorta			
4 Stricture of esophagus	1		1
5 Rupture of esophagus	1		1
6 Tumor of lung	1		1
b Suppuration of lymph node		2	
Total	23	5	18
II Chronic abscess			
a Abscess tuberculosis	3	-	1
C Acute diffuse mediastinitis			
I Pneumonia	14		14
II Peritonitis			2
Total	16		16
Total	60	12	48

In mediastino pericarditis there is often a difference in the blood pressure of the two radials when the patient is recumbent the pressure in the left being the lower This is not observed when he is standing In certain of such cases a systolic retraction of the left scapular region or even of the entire left chest may be observed

In the *Differential Diagnosis* it must be borne in mind that while chronic superior mediastinitis is usually syphilitic the form known as mediastino-pericarditis is almost invariably tuberculous or of focal origin In the mediastinitis of childhood tuberculous lymph nodes are always to be thought of In adults three conditions must be differentiated (1) aneurysm with its typical pulsation localized expansile sac brassy cough ringing aortic second sound and paralysis of the recurrent laryngeal nerve (2) malignant tumor with its substernal pain paroxysmal cough often without sputum area of retrosternal dullness dyspnea and occasional inequality of pupils and (3) tracheobronchial adenopathy which in adults is seldom sufficiently marked to produce the symptoms of mediastinitis (leukemia Hodgkin s disease)

Radiology is of great value here as in other diseases of the mediastinum the oblique view from the left posteriorly to the right anteriorly being the most satisfactory A mottled or a striped thickening is seen in the normally light area behind the heart or above the great vessels This may take the form of fibrous bands crossing the mediastinum in every direction or an indefinite mottled mass may be seen in the upper clear space The heart outline may be indistinct because of a dark shadow bounding it on all sides and the movements of the apex may be definitely limited Tumors give a large shadow of a uniformly opaque irregular mass

The *Treatment* is that of the disease which produced the mediastinitis Syphilis which has advanced unrecognized or unheeded to this stage is difficult to treat effectively although intensive medication may lead to an amelioration of the symptoms Here also the surgical procedure of opening the sternum with the object of relieving the acute pressure symptoms of indurative mediastinitis has been attempted with a fair degree of success[17]

Other Diseases of Mediastinum

Mediastinal Emphysema has been reported occasionally in the past but always as the result of some gross injury to the air passages or esophagu such as penetrating wounds perforating ulcer or the rupture of a bronchus A tympanitic percussion note is heard over the anterior chest wall and the heart beat can be neither heard or felt Usually a crackling sound synchronous with the pulse wave may be heard over the mediastinum

phragm should be mentioned Pressure symptoms usually are absent but the condition may be recognized by aid of a roentgenogram made after a contrast meal This is discussed in greater detail in Vol II Chapt II

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Spontaneous emphysema of the mediastinum has been described by Hamman[10] who believes that it is of relatively frequent occurrence The explanation offered is that in an apparently healthy person a wall of an alveolus in the lung becomes attenuated and so weakened that it ruptures whereupon the escaping air travels along fascial lines to the mediastinum This accident may occur when the patient is at ease and making no effort The air may remain in the mediastinum to be absorbed gradually or it may travel upwards and produce emphysema of the subcutaneous tissues of the neck and chest although Hamman did not see the latter phenomenon in any of his cases Pneumothorax occasionally complicates the picture and the author just quoted thinks it not unlikely that this condition is sometimes the result of unrecognized mediastinal emphysema

The pain produced usually is substernal and as a rule, is extremely severe It may radiate to the back neck or shoulders seldom to the arms The temperature pulse and respiratory rate are altered little if any and there is no evidence of shock The dullness normally encountered over the cardiac area is replaced by a hyperresonant percussion note Hamman describes a peculiar distinctive sound characterized as crunching crepitant or crackling heard over the heart synchronous with its contractions He states that when once heard the nature of this sound could never again be confused The patient may hear the sound and it may be audible at some distance from the patient s chest As a rule the leucocyte count is not elevated The roentgenogram may give a characteristic picture In the lateral view the tissues between the heart and anterior wall of the chest are seen to be filled with air or from the anterior posterior view a characteristically sharp distinct line may be seen running parallel to the border of the heart Ordinarily the air is absorbed eventually If however the increasing pressure becomes so great as to threaten collapse of the veins and auricles then as has been done successfully in traumatic emphysema an incision can be made to permit exit of the air

Emphysema of the lungs and mediastinum extending to the subcutaneous tissues of the neck was a striking complication encountered in the influenza epidemic of 1918[18]

Hemorrhage into the mediastinum occasionally follows fracture of the sternum or other trauma and in such instances not infrequently is followed by an abscess In certain hemorrhagic diseases bleeding may occur into the mediastinum Hemorrhage from aneurysm is fairly frequent usually being a fatal accident

Hernia of the abdominal contents through an opening in the dia

CHAPTER VI-A

CLINICAL ALLERGY

By J WARRICK THOMAS

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Introduction

In the past three or four decades the recognition of the various manifestations of allergy has advanced and the handling of such problems has been facilitated by this broadening of knowledge in both medical and lay circles The term allergy is now used in the everyday vocabulary of many children as well as adults The practice of allergy as a factor in general medicine has passed its embryonic development and has assumed its just position in our medical armamentarium It is imperative that the clinician know the diseases and symptoms which may be of allergic origin

It is still more important however to be able to see the picture as a whole and not to ascribe to allergy those entities of different causes Allergy must be considered one of the fundamental factors in the causation of disease It is primarily a chemical problem and when one comes to the final analysis in most diseases the summation of the problem is a result of chemical action in the

the extraction of them When in 1894 at the meeting of the International Congress on Hygiene and Demography at Budapest Von Behring and Roux reported the remarkable results of the use of diphtheria antitoxin each doctor attending the meeting returned home carrying with him a small vial of the precious serum

Now began a period of what might almost be termed feverish activity in experimental laboratories in an effort to know more of these interesting phenomena of toxin formation antitoxin production and immunization Similar activity developed in the commercial pharmaceutical laboratories where methods were soon developed for the large volume production of therapeutic antitoxin As concerns allergy we now reenter a period of historical observation with no serious effort toward the elucidation of recorded observations In 1894 Flexner wrote animals that had withstood one dose of dog serum would succumb to a second dose given after the lapse of some days or weeks even when this dose was sublethal for a control animal Victor C Vaughan records that at about this time a large pharmaceutical house in Detroit preparing antitoxins and testing their potency on guinea pigs found that if guinea pigs were used more than once for this study curious and unexpected things occurred Many of the pigs would suddenly die following repeated inoculations Finding these animals unreliable and therefore useless after a single test they sold them as used pigs at a very small price to the laboratories of the University of Michigan Medical School but these pigs were found dear at any price since reactions proved to be quite unreliable when they were used as experimental animals

During this period Theobald Smith had observed similar curious reactions and he too offered no explanation but he mentioned the phenomenon in conversation with Ehrlich who at once put his student Otto to work upon the problem The careful investigations of Otto over a period of several years on what he chose to term the Theobald Smith phenomenon were published subsequent to the work of Richet which marks our next milestone

Richet and Hericourt in 1898 placed another historical landmark in that they recorded their observation that dogs treated with eel serum which is in itself toxic could be killed with a second injection of the serum but with an amount too small to injure normal control animals on second injection The lethal dose on second injection could be much smaller than the minimal lethal dose on first injection Here again they merely recorded an interesting observation with no attempt at explanation A few years later however Richet and Portier returned to the study pursuing it until they had succeeded in evolving their theory of anaphylaxis

Richet and Portier from their studies of actinocongestin the urticating substance of actinia the sea anemone enunciated two conclusions which are fundamental to our knowledge of anaphylaxis and allergy The first of these

body tissues In the consideration of all diseases it is just as important to evaluate the susceptibility of tissue to reaction as it is to recognize the agents that are immediately responsible for such reactions

In the following discussion we are attempting to review the growth of allergy from its infancy to its maturity and to analyze the frank allergic manifestations, those manifestations generally appreciated as well as those less common The application of the appropriate therapeutic procedure is considered

Historical

Although in its modern form clinical allergy is a development of the last thirty or more years scattered observations similar to those which form the basis for our present understanding were recorded much earlier Indeed the earliest was over one hundred years ago As early as 1839 Magendie described sudden death in dogs which had been injected repeatedly with egg albumin

Isolated observations such as that of Magendie and others which have followed it make it difficult to establish precise dates for the conception and birth of the science of immunology of which clinical allergy is an off shoot but clinical or experimental observations which are recorded merely as curiosities with no follow up studies or other attempts at explanation are really no more than historical land marks for which the recorder deserves credit only as an alert observer rather than as an intelligent investigator With this as a criterion we can trace the story of anaphylaxis and immunology back in unbroken sequence to the period from 1882 to 1889 At that time this branch of medicine was conceived in the sense that the germ was first implanted which made possible its birth at the opening of the twentieth century

During these years in the eighties Henry Sewall then Professor of Physiology at the University of Michigan was conducting a series of observations on snake venom At last he succeeded in immunizing pigeons against this poison The work of Sewall was carried farther in the investigations of Calmette and of Physalix and Bertrand who prepared an antitoxin Very shortly Roux and Yersin showed that the poison produced by the diphtheria bacillus is similar to that of snake venom This was very quickly followed in 1894 by the epochal discovery, independently made by two investigators Von Behring and Roux of diphtheria antitoxin

During the next eight years or more scientific interest was centered on toxins curious poisons elaborated by living tissues which were secreted or could otherwise be separated from the undamaged living structures and against which an antibody could be produced by the process of immunization Sewall and Calmette had shown toxins to be of animal origin Roux and Yersin had demonstrated that they were produced by bacteria Ehrlich had proven a vegetable origin in

The term *allergy* proposed by von Pirquet and meaning altered activity or altered reactivity is clearly descriptive and requires the adoption of no single theory Von Pirquet used the term merely to signify altered reaction but in his writings he implied the belief that an antigen antibody reaction was the basis of the phenomenon Doerr extended von Pirquet s definition to include all forms of changed reaction capacity irrespective of whether or not an antigen antibody reaction could be demonstrated It is unfortunate that Coca has given an entirely different interpretation to the term from that originally intended by von Pirquet since this has tended to obscure the issue Coca classified as anaphylaxis those phenomena in which an antigen antibody reaction may be demonstrated and as allergy that phase of hypersensitiveness in which such a reaction appears not to be present This is quite the reverse of von Pirquet s intention

The term *atopy* suggested by Coca to designate what are commonly known as the clinical allergies like the term allergy commits the user to no special theory The word merely means strange disease Coca emphasizes the hereditary nature of human clinical allergy in contrast to the apparently non hereditary nature of experimental anaphylaxis If we are to judge the disease by the frequency of its incidence we shall see as we progress that clinical allergy is by no means a strange disease

Protein poisoning proposed by Victor C Vaughan was an appropriate term as long as it appeared that anaphylaxis or allergy could be manifested only against foreign proteins The hapten theory elaborated by Landsteiner made it still possible to include hypersensitiveness to non organic substances such as arsphenamine quinine aspirin and iodide when introduced into the body as phenomena of protein sensitization or protein poisoning but if we are to include in the clinical allergies contact dermatitis to such varied substances as the heavy metals synthetic chemicals and plastics protein poisoning is no longer a sufficiently inclusive term although we might still hypothecate a combining of the foreign substance with the protein of the tissue cell

All in all the term *allergy* is the most appropriate so far and we shall use it in this discussion in its original sense as proposed by von Pirquet and elaborated by Doerr Furthermore in the English speaking countries this term has come into such general use that it would be unwise at the present time to propose another It is also the accepted terminology in Spain and South America In France *anaphylaxie* is used alternatively while in Germany *Überempfindlichkeit* (hypersensitiveness) is the customary term

The Chemistry of Antibodies

We still discuss the mechanism of the allergic reaction in terms of Ehrlich s concept of immunity It has been said that we know antibodies not by what

was that a substance which in a stated dosage was not harmful on first injection, might be both harmful and even lethal on second injection in the same dosage or even in much smaller amount The second conclusion was that a certain time interval must elapse between the two parenteral injections It is true that these workers were dealing with a naturally toxic substance although in sub-toxic dosage but the two principles which they formulated, were basic in anaphylaxis It remained for Arthus to demonstrate that the same two principles applied to the parenteral administration of non toxic substances in his description of the familiar Arthus phenomenon by which rabbits may be made hyper susceptible to horse serum following repeated injections

The work was then carried along rapidly by a number of investigators notable of whom were Otto in Germany and Rosenau and Anderson in the United States These investigators demonstrated the complete independence of this phenomenon from toxin or antitoxin the phenomenon of antianaphylaxis following repeated small injections the incubation period of about ten days the specificity of the reaction the transference of hypersensitiveness from mother to offspring the varied nature of possible antigens (animal vegetable bacterial) and the extreme delicacy of the reaction Rosenau and Anderson were able to sensitize a guinea pig with as small an amount as one millionth of a cubic centimeter of horse serum

The observations made in Europe by von Pirquet and in America by Victor C Vaughan indicating that sensitization may occur to bacteria as well as to other foreign proteins laid the groundwork for subsequent developments in our knowledge of bacterial allergy

A review of the later developments in experimental anaphylaxis would be out of place in the present discussion but we must mention briefly the divergent terminologies which have been proposed and come into use and which have resulted in considerable confusion in classification

Terminology

The term *anaphylaxis* proposed by Richet and Portier should connote the loss of a protective mechanism in contradistinction to the prophylactic production of a protective mechanism in immunity It has been subject to much criticism as being too definitive and committing the user to a theory explaining the mechanism which may not be the true explanation As long however as we continue to think in terms of Ehrlich s side chain theory the term anaphylaxis is rational The antibodies of a hypersensitized animal are fixed to the tissue cells with the result that combination with the antigen damages the cells The antibodies of an immunized animal are free in the circulating fluids and by combining with the antigen prevent the latter from attaching itself to the tissue cells

What takes place during the anaphylactic reaction remains rather obscure We now know (1) that histamine exists in loose combination in many living tissues ( ) that in the allergic response there is a noteworthy increase of histamine or some substance closely resembling it in the blood and in the tissues participating in the reaction and (3) that histamine causes tissue responses which are indistinguishable from those of anaphylaxis

We may presume therefore that the reaction between antigen and the globulin antibody within the cell(?) produces damage and consequent release of histamine and that the latter is in turn responsible for the capillary hyper permeability smooth muscle spasm and other responses which produce symptoms

Early Observations

The earliest description of hay fever as we understand the condition today is to be found in the writings of Botallus (1565) His contribution and those of several who followed him up to the time of Bostock merely mention the condition as a curious observation Bostock (1819) first described the disease as a clinical entity and in his writings there is evidence that the laity of his time suspected that the inhaling of some product from grains and grasses was the responsible factor He himself combated this idea Elliotson (18 9) is credited as the first to state his belief in a scientific paper that hay fever is due to the pollen of flowers Blackley of Manchester England demonstrated with a series of painstaking experiments the relationship of pollen to the causation of hay fever (1873) In these studies he used many of the methods which are in common use today such as the collection of pollen both directly and from the air on pollen plates skin testing and mucous membrane testing However since Blackley s studies offered nothing special in the direction of treatment they attracted little interest until they were confirmed by Dunbar an American working in Hamburg who in 1903 expressed his belief that hay fever was due to the specific action of a toxin similar to that of diphtheria and tetanus formed in the pollen and deposited on the nasal mucosa He produced a so-called antitoxin by the immunization of horses against an albuminous extract of pollen This received a great vogue in treatment over a period of almost ten years Pollantin as he named his so-called antitoxin was administered locally on the nasal and conjunctival mucosa Weichardt working in Dunbar s laboratory proposed another remedy graminol altogether different but based upon the same theory He believed that cattle fed upon the grains responsible for hay fever would immunize themselves against the toxin Graminol therefore consisted merely of normal serum from cattle fed large amounts of timothy and other grasses Since the premise in both of these methods was erroneous in that there is no toxin formed these therapeutic measures failed to relieve and eventually lost favor

they are but by what they do Within the last ten years, however, much has been learned of their chemistry and mode of manufacture

Sabin employing the tracer bullet principle, has tagged foreign proteins by combining them chemically with a red dye which may be identified microscopically in tissues After injection this dye is deposited in the cells of the reticuloendothelial system As it gradually disappears antibodies for this protein dye hapten combination appear in the blood This is the best evidence so far that antibodies are made in the cells of the reticuloendothelial system In the blood they are in the globulin fraction There is evidence that antibodies are protein modified globulin The molecules are large The molecular weight of blood globulin varies in different animals from 160,000 in the human the monkey and the rabbit to 990 000 in the pig cow and horse It is interesting that the pneumococcus antibody of the rabbit has less than one sixth the molecular weight of the pneumococcus antibody of the horse, but that both exert very much the same action on the pneumococcus This suggests that only a portion of the anti body molecule is the active element in the antigen antibody reaction

Today we can almost say that we have seen antibodies They are large enough to cast a shadow in the electron microscope With this apparatus it has been found that typhoid antibodies are elongate, probably rod shaped and are about 275 Angstrom units long 35 wide

We even have a fair idea of how antibodies are made The ordinary protein molecule is rather long and narrow but rolled upon itself like a spiral nebula or an unused stair carpet Some investigators believe that both ends roll up inde pendently The first stage in denaturization of protein consists of a process of unfolding or straightening out In the manufacture of antibodies it would appear that a globulin stimulated by the presence of a foreign protein, unfolds Possibly both the globulin and foreign protein do so Reactions occur at the interfaces of these two proteins probably chiefly at the ends of the unfolded molecules There is probably some chemical reaction between the two which results in a permanent templating of the serum globulin to fit certain characteristic valences of the foreign protein This templating is the permanent change which enables the antibodies thereafter to combine promptly with the specific antigen It is pre sumed that the templating occurs chiefly inside the reticuloendothelial cells during the process of globulin manufacture

Artificial antibodies have been made in vitro Serum globulin is denatured by change of pH or of temperature or in other ways and when exposed to the antigen The antigens used experimentally so far are haptens an azo dye and type III pneumococcus polysaccharide The denaturing environmental influence hydrogen ion concentration temperature etc next is slowly reversed to normal and the antigen is removed by dialysis As the globulin refolds it presumably assumes a configuration complementary to that of the antigen

of clinical manifestations has been shown to be due in part at least to allergy including particularly urticaria eczema and contact dermatitis In recent years evidence has been adduced indicating that allergy may play a part in certain other organic disturbances These will be discussed later

Before leaving the discussion of the historical and more theoretical aspects of clinical allergy it would be well to clarify to a greater degree the relationship between experimental anaphylaxis and clinical allergy as it is understood today The similarity between clinical allergy and experimental anaphylaxis is striking All of our clinical progress in this field of medicine has developed as a result of recognition of this similarity Apparent dissimilarities have been taken by some to indicate a basic difference requiring separate classification The leader in this group is Coca who elaborates three fundamental points of difference between experimental anaphylaxis and clinical allergy as follows (1) anaphylactic anti bodies cannot be demonstrated in human hypersensitiveness and atopic reagins are not observed in experimental anaphylaxis (2) natural human hypersensitiveness cannot be produced at will as is the case in experimental animals nor when it exists naturally can it be abolished totally by desensitization (3) an hereditary factor appears to be predominant in human allergy which is not the case in experimental anaphylaxis[3]

The present writer feels for reasons which will be presented later that as our knowledge of experimental anaphylaxis and clinical allergy grows the two will be found to approach each other steadily and to have a common fundamental basis with points of dissimilarity easily explainable by secondary factors As a matter of fact all knowledge of clinical allergy is based primarily on studies of experimental anaphylaxis Shortly after the turn of the century von Pirquet and Schick explained sudden deaths after diphtheria antitoxin and the delayed urticaria known as serum sickness by their resemblance to the laboratory phe nomenon All of clinical allergy has evolved from this early observation

Prevalence and General Characteristics

Scheppegrell in 1916 estimated that from 1 to 2 per cent of the population suffer from hay fever at some period of the year[13] The apparent increase in this malady in the last 20 years probably is a true one and due to progressive destruc tion of forested areas with resulting increased cultivation and increased weed production Hoffman estimates over one half million sufferers from asthma in the United States Spain and Cooke[14] estimate from their New York survey that 3 5 per cent of the population has hay fever or asthma at one time or an other Piness and Miller[15] found 4 4 per cent incidence of hay fever in a western town of 3 000 population and 3 per cent in anothe town of 1 000 21 6 per cent of the hay fever patients also had asthma

The first suggestion that hay fever might be due to a process similar to anaphylaxis without the presence of a natural toxin was made by Wolff Eisner[1] in 1906 Following this and the demonstration by Auer and Lewis (1910) that anaphylactic shock as observed in guinea pigs is associated with bronchospasm the suggestion was made by Meltzer (1910) that asthma may be a form of human anaphylaxis[2] Others undoubtedly had had similar ideas, for work was in progress at that time on the treatment of hay fever along the line of allergy as we today understand it Curtis in 1900 had attempted the administration of ragweed extract hypodermically, later orally Scheppegrell had applied the dried pollen to the nasal mucosa, but credit for the initiation of hay fever treatment, as it is used today goes to Noon and Freeman of England[4 5], who in 1911 first reported the results of active immunization or desensitization with pollen extract

Perhaps the next clinical phenomenon which came under scrutiny as a possible anaphylactic reaction was drug idiosyncrasy This was first studied seriously from this angle by Jadassohn Following his work there were many conflicting studies until the observations of Obermeyer and Pick and of Landsteiner, who demonstrated that native proteins could be combined chemically with other substances such as iodine and azo compounds to form new proteins to which experimental animals react specifically while failing to react to the original protein with which the chemical is combined There has been much conflicting experimental work in drug idiosyncrasy, but one can say now that it has been proven experimentally that this is an anaphylactic phenomenon And, clinically drug idiosyncrasy does fall in the allergic group, in that the individual exhibits *altered reactivity* to the drug in question

With the concept enunciated by Wells[6], that inasmuch as the anaphylactic reaction is associated with smooth muscle spasm and since smooth muscle pre ponderances in the vascular system vary in different species of animals, the idea developed that anaphylactic or allergic manifestations may present themselves in different organs or tissues of the body In guinea pigs there is an over-development of smooth muscle in the bronchial tissue, in rabbits in the pulmonary vessels and in dogs in the hepatic arteries Anaphylactic reactions vary accordingly in these animals This idea has been elaborated further by Coca[7] in the suggestion that the location of the shock tissue, possibly the sensitized tissue may vary in different individuals

Schloss (1912) called attention to urticaria angioneurotic edema and eczema as being associated with food idiosyncrasy[8] Duke (1921) showed that food allergy may be responsible for indigestion and abdominal pain[9] In 1922 he reported genitourinary symptoms due to allergy In 1922 Vaughan described mucous colitis as a result of food allergy[10] Pagniez Vallery Radot and Nast (1919) appear to have been first to suggest allergy as a possible cause of migraine which was proven experimentally in 1927 by Vaughan[11] Since 1910 a variety

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some degree allergic is the phenomenon in essence a disease or is it a physiological variation? If the statistics are correct the question is no longer why do some become allergic ? but why do not all individuals manifest allergy ?

Adkinson[19] Cooke and Vander Veer[6] Spain Cooke Balyeat[1] and Weiner have shown an hereditary predisposition to allergy the evidence of the investigations indicating an adherence to the Mendelian law This work was all done on cases of *major allergy* Vaughan has found in his series of *minor* allergics that the inheritance is about equal between the minor allergics and those without allergic manifestations He suggests the following explanation for these apparently divergent observations

The primary requisite for the production of the anaphylactic state in the experimental animal is the introduction of foreign protein into the blood stream Walzer and his associates' have shown that in the normal human food allergens pass the barrier of the intestinal tract and the liver and enter the circulation still sufficiently undigested so that they may be recognized by biological test This is in contradiction to the generally accepted understanding of the physiology of protein digestion but Walzer s work appears to be correct If therefore a condition normally exists in humans comparable to that considered requisite in animals for the production of the anaphylactic state the surprise is that all individuals do not become allergic at one time or another Possibly if all individuals lived long enough they would do so The inheritance or predisposition appears to be the same among allergics and non allergics except that among those who are frankly allergic the inheritance is heavier Allergy is not so much a pathological state as it is a pathological exaggeration of a normal physiological response Why some individuals respond with symptoms which we recognize as allergic while others do not remains to be explained

Very interesting work was reported in 1934 by Simon and Rackemann[**] which may be interpreted as confirmatory of the hypothesis presented by Vaughan One of the arguments advanced by some authors for their belief that clinical allergy is different from experimental anaphylaxis is that while animals may be sensitized at will it is most difficult intentionally to sensitize individuals even allergic individuals Brunner[3] concluded as recently as 1932 that it is difficult to sensitize human beings actively to common atopens Nevertheless it is a matter of current observation that persons may be sensitized easily to horse serum as evidenced by the development of serum sickness[21] In 1934 Jones and Mote[3] reported no difficulty in sensitizing humans to rabbit protein and Simon and Rackemann reported similar experiences with guinea pig serum They found no outstanding difference between atopic and non atopic persons as regards the ability to sensitize them to guinea pig serum They remarked the difference between our subjects artificially sensitized by intracutaneous dosage and our patients naturally sensitive to foreign substances of various kinds may

Spain and Cooke estimate that 7 per cent of the population suffers from frank allergy in one form or another Vaughan[16] in a survey of the entire population of a small Virginia town comprising 508 individuals found 10 per cent frankly allergic Five and three tenths per cent of the population had had frank hay fever 3 3 per cent asthma, 2 9 per cent vasomotor rhinitis, 4 9 per cent urticaria, 0 6 per cent allergic eczema 3 1 per cent allergic headaches 4 5 per cent gastro-intestinal allergy 0 39 per cent gave a history of angioneurotic edema Many in this series presented more than one symptom The total of 10 per cent is higher than the 7 per cent of Spain and Cooke This is explained by the observation that Vaughan s survey was made 8 years after that of Spain and Cooke when we had a clearer understanding of allergic manifestations, and more symptom complexes were included in this category This applies especially to contact dermatitis and allergic headache Spain and Cooke limited their cases to hay fever asthma and urticaria

Vaughan s survey attempted to differentiate the frankly allergic person from the individual who at some time in his life has had some minor allergic manifestation which usually had not been persistent and had not required the individual s consulting a physician He divides allergic individuals into two groups the major allergic the 10 per cent previously mentioned and the minor allergic, those who at some time in the past have had some low grade temporary or intermittent allergic symptoms This latter group was found to comprise 50 per cent of the population making a total of 60 per cent either major or minor allergic There is a very interesting differentiation between the two groups The major allergic usually was sensitized to some allergen with which he came into frequent or daily contact and therefore was unable to recognize it as the cause of his symptoms The minor allergic was sensitized to some substance with which he came into only occasional contact and which he had little difficulty in recognizing as the cause He also had little difficulty in avoiding it as a rule thereby relieving himself of his symptom Among the foods the major allergic was likely to be sensitized to wheat egg milk or some other staple while the minor allergic reacted to occasional and seasonal foods such as strawberry, tomato cantaloupe and cucumber This appears to be the outstanding difference between the major or unfortunate allergic and the minor or fortunate allergic

Rowe[17] has observed in a survey of college students that 31 per cent gave a history of definite allergic disturbances probably due in whole or part to specific foods Vaughan observed 43 per cent in his survey with some history of food allergy Pipes[18] survey is also in keeping with these observations

If over half the population becomes allergic to some substance at some time in life allergy can no longer be considered a strange disease', meaning uncommon Indeed this apparent high frequency, if correct raises the question as to the fundamental nature of the malady If the majority of persons is to

standing of anaphylaxis an understanding which may require radical revision in the future

In his studies on *the human constitution* Draper[28] divides the whole of the human constitution into four parts or panels Drawing an analogy to the oriental practice of spreading a portrait across four panels of a screen each panel representing a separate portion of the complete picture he divides his constitutional screen into a morphological panel a physiological panel an immunological panel and a psychological panel Draper obviously recognizes the importance of immunological processes in the body giving it a tantamount position with the three other dominant traits One might be tempted to suggest a fifth panel the allergic but this rightfully belongs within the immunological picture How large a portion of this picture it occupies in our daily existence is suggested in the foregoing discussion

Clinical Allergy

We have seen that allergy may be a factor in the causation of such apparently diverse conditions as asthma hay fever urticaria eczema migraine and non ulcerative colitis It has also been found to play a part in the causation of a *number of other syndromes usually of obscure or multiple etiology Sometimes it is only one of several factors at others the chief factor and yet again not a factor at all In this group of maladies in which it has been proven that allergy must be considered as a possible factor may be mentioned allergic cough or bronchitis (Colmes[7] Van Ordstrand and Ernstene[8] Thomas and Taylor[9] and Waldbott[30]) canker sores (Beecher[31] and Thomas and Wofford[32]) trichophytosis (Sulzberger[33]) purpura (Alexander and Evermann[34] and Thomas and Forsythe[35]) erythema multiforme (Lowe[36]) epilepsy (Wallis Nicol and Craig[37] and Clarke[38]) Meniere s disease (Duke[39]) cyclic or periodic vomiting (Thomas and Kmell[40]) agranulocytosis Loeffler s syndrome (Hansen Pruss and Goodman[41]) periarteritis nodosa genitourinary allergy (Thomas and Wiksten[42]) and selected cases of progressive myopia Other conditions in which as yet uncompleted evidence of an allergic factor of greater or lesser importance has been presented include angina associated with tobacco sensitivity (Harkavy[43]) thromboangiitis associated with tobacco sensitivity (Sulzberger[44]) and status thymicolymphaticus (Waldbott[45])*

One might almost paraphrase the dictum of Fournier dean of early syphilographers in saying allergy is the great imitator One might better call it *the great intruder since allergy insinuates itself into and colors the clinical* picture of such a wide variety of otherwise clear-cut symptom complexes rheumatic fever atrophic or rheumatoid arthritis serum sickness trichiniasis ascariasis etc

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be merely a difference in degree" This, obviously, represents a line of thought analogous to that presented above

These observations, correlated with those of Vaughan that minor allergics usually are sensitized to substances with which they come into only occasional contact raise interesting speculation on the relationship between experimental anaphylaxis and clinical allergy As the writer sees it there is no fundamental difference The apparent difference depends upon the substance to which an individual becomes allergic Even so, the difference does not lie in the chemistry of the allergen but in the factor of degree or length of exposure Richet and Portier injected into their experimental dogs a substance with which the dogs had never come in contact Most of the early work on experimental anaphylaxis in guinea pigs was done with substances such as horse serum and egg white substances with which guinea pigs usually do not come in contact If other substances antigens with which guinea pigs were naturally in constant contact, had been used in the early work on anaphylaxis the observations would have been far different Experimental anaphylaxis is analogous to minor allergy, and it is analogous to the type of sensitization that is produced with therapeutic horse serum and in the experiments of Jones and Mote and of Simon and Rackemann Brunner was unable to sensitize individuals to orris root, because it is a substance with which we usually come in rather constant contact Simon was unable to sensitize humans against egg white for the same reason but he had no difficulty in sensitizing them against guinea pig serum Nor is there difficulty in sensitizing guinea pigs against egg white And yet apparently the only fundamental difference between minor allergy and major allergy is in the degree or duration or frequency of exposure In other words here is circumstantial and indirect evidence that clinical allergy and experimental anaphylaxis depend upon identical processes

It would seem that when the tissues of an animal or human being come in contact with a foreign substance especially a foreign protein, with which natural contact is established only occasionally sensitization may be accomplished with relative ease When contact is established with a foreign substance with which the animal comes into frequent or daily contact sensitization is estabished only with difficulty Yet even in this case it sometimes is established, and it is this group of humans who form the large bulk of the major allergics or cases of clinical allergy, which we shall discuss in the next section The intensity of allergic inheritance may explain the greater ease with which major allergics become sensitized It is interesting to theorize concerning the difference between occasional and frequent contact substances and to suggest that the body usually does not become sensitized to frequent contactants because it is constantly desensitizing itself with them and that only occasionally does this protective mechanism break down However this is but theory based upon present day under

standing of anaphylaxis an understanding which may require radical revision in the future

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in which the allergic factor acts in these diverse disease entities When it is of sufficient importance this will be found elsewhere in the discussions of the diseases considered The remainder of this section therefore will be devoted to a discussion of the general methods of allergic study and treatment as they have been developed and improved upon within the last ten or more years As a rule the methods apply equally to all cases in which an allergic factor is suspected irrespective of the clinical picture

Improvements in Diagnostic and Therapeutic Methods

The early French workers desiring to do skin tests, made a paste of the natural substance under suspicion and applied it to the abraded skin The preparation of purified concentrated protein extracts has been developed since especially in this country by various workers most notable of whom has been Coca whose interest in this field still continues Noon and Freeman working with relatively low atmospheric concentrations of grass pollen established a pollen unit for therapeutic purposes and a graduated system of dosage based thereon Walker Cooke and others, taking up the problem in the United States and working on the Atlantic seaboard where the ragweed pollen concentration is relatively very low found comparable preseasonal dosages to be adequate Koessler Duke and others working in the Mississippi basin the great hotbed of ragweed where pollen concentrations are far higher than on the Eastern seaboard found it necessary to increase materially the preseasonal dosage In the large Eastern cities the top or final preseasonal dose of 2 000 to 4 000 pollen units often was sufficient Waldbott has given very large doses of pollen extract 40 000 to 50 000 unit dosage with good results In the Mississippi basin a required dose of 20 000 is not uncommon The pollen unit represents the extract of one millionth of a gram of dry pollen This increase in dosage resulted in definite improvement in therapeutic results It is now being used by many on the Eastern seaboard The fifteen dose treatment set as it has been marketed provided a highest dose of from 2 000 to 4 000 pollen units Most of the manufacturing concerns now supply extra amounts for increased dosages

Early in the development of pollen treatment it was believed that desensitization therapy must be begun and completed prior to the onset of the pollen season Treatment should not be given during the season because of the risk of systemic anaphylactic reaction Following Vaughan s observation (1923) that treatment may be given during the season both to those who have had preseasonal desensitization and to those who have had none provided the desensitizing dose is kept extremely small and given more frequently[46], this method of coseasonal treatment has come into general use

Aaron Brown[47] noticed that individuals sensitive to horse dander, who must

continue contact with horses and who are therefore desensitized to horse dander perennially for several years sometimes lose their sensitization completely apparently as a result of the long continued treatment. Believing that there was a possibility that similar results could be accomplished in pollen allergy he inaugurated the perennial method of treatment. The perennial treatment possesses certain advantages. It avoids the annual preseasonal intensive desensitization reduces the necessary total number of inoculations gives slightly better results as a rule and *after 3 or 4 years of treatment often enables the patient to* go another 3 or 4 years without desensitization treatment. Up to the present the writer has seen a few apparent total cures but the permanency can only be determined after the lapse of considerably more time.

Summarizing the improvements in the diagnosis and treatment of pollen allergy we may say therefore that the preseasonal dosage has been increased where necessary coseasonal and perennial treatments have been developed and *in addition very careful botanical and pollen surveys have been made at repre*sentative areas scattered through the United States[48, 49] so that today we know of a much larger number of actual allergens causing pollinosis and as a consequence are more likely to use the appropriate antigen thereby improving results.

There have been comparable developments in the study and treatment of food allergy. Alexander[50] probably first called attention to the deficiencies of the skin test method especially in food allergy. Positive reactions often are observed *to foods which are found to be innocuous and sometimes foods which actually* cause trouble fail to give positive diagnostic reactions. The reliability of the skin test has been roughly estimated at about 50 per cent especially as regards foods. Of course the fact that 50 per cent of the allergenic foods can be discovered promptly by this method establishes its value as the point of departure in the study.

Further improvements have been elaborated in the direction of discovering the 50 per cent of substances which cannot be found by the skin test method. The scratch method of testing was improved by Cooke[51] by the intracutaneous *method. Quite an argument waged for some time as to the relative merits of* the two methods which was apparently settled by Fineman[5] who established that the intracutaneous method is on the average one hundred times more reactive than the cutaneous. An intracutaneous test solution one hundred times more dilute than a scratch solution would then have little or no advantage over the latter. Since this was often or usually the case in early extracts there was justification for difference of opinion. The present method employed by many consists in preliminary scratches to be followed in the case of apparently negative or doubtful allergens by intracutaneous testing with a relatively much more *concentrated extract. This has decreased the number of false negative reactions* at the same time preserving the safety factor of the scratch method. Foods or

other allergens which have shown up already as positive by scratch, need not be repeated intracutaneously

Another method which has been developed to obviate the false negative reaction has been the *elimination diet* of Rowe[17]. The patient is placed on a stated diet made up of a few foods which have been found to be infrequently allergenic. There is a series of such diets so that, if the patient does not respond to the first, others may be tried successively. One diet often is found on which he does well, after which individual foods are added gradually. Many allergists prefer to formulate the trial diet individually for each patient, based upon the results of antecedent skin testing.

Realization that many foods are related[18] genetically has tended also to circumvent the false negative reaction. Thus if a positive reaction has been observed to Irish potato with a negative to tomato, the patient is instructed to watch the effects of eating tomatoes, red and green peppers and eggplant, which are biologically closely related to the Irish potato. In this way the patient himself discovers additional offending foods. In allergic practice foods originally were classified merely from a culinary point of view into nuts, fruits, leafy vegetables, starchy vegetables and the like. The genetic classification of Vaughan brings out the group relationships. Mustard, turnip, cabbage, kale, Brussels sprouts, broccoli, cauliflower and rutabaga are all cousins. The chief difference lies in the fact that the edible portion represents a different part of the plant: the mustard is the seed; kale and cabbage, the leaf; turnip and rutabaga, the root; broccoli, the stem; Brussels sprouts, the bud; cauliflower, the flower. Almond is much more closely related to peach than it is to the other nuts just as the peanut is a member of the pea bean family and is in reality a goober pea. Spinach is not at all related to lettuce or cabbage or turnip leaves but is a close cousin of the beet. Cucumber and cantaloupe are so closely related that they possess an identical protein, cucurbitin. The same is true of amandin which is found in both peach and almond.

The food diary[48] also enables one to detect offending foods which have failed to give positive skin reactions. The patient keeps a daily record of all foods and other substances taken internally, recording them by a method of checking on a special form which subsequently may be read easily. He also records the days on which he has symptoms. Analysis of the chart often enables one to spot offending foods which appear to have been eaten only prior to attacks.

The foods giving false positive skin reactions may be eliminated gradually in the course of treatment by dietary trial. After the patient has been satisfactorily relieved, he partakes of one prohibited food at a time in addition to his basic diet, thereby discovering which ones do and which do not produce symptoms.

It becomes apparent that allergic study and treatment involves far more than the application of sensitization tests. Since one usually is sensitized to a

number of allergens at the same time it sometimes requires months of painstaking collaboration between doctor and patient before all of the etiological factors have been recognized and successfully eliminated

There is an inclination to feel that debate as to the allergic etiology of asthma hay fever and kindred diseases is of recent origin There are still rhinologists who insist that local nasal pathology is the chief precipitating factor Many other non allergic causes have been proposed and insisted upon However this is not a new discussion It commenced as early as 1830 when Elliotson first demonstrated pollen as responsible for summer asthma and hay fever At that time Bostock the man who appears to have been first to describe the disease entity took exception to the theory The argument still continues but with decreasing intensity

Rackemann[53] has done much to clarify the discussion in dividing the allergic diseases into two groups the extrinsic and the intrinsic The former are clearly allergic due to contact with extrinsic factors derived from the environment Usually exposure is by either inhalation ingestion or cutaneous contact Intrinsic allergy apparently due to some metabolic or infectious processes in the body itself may or may not be allergic although an allergic factor often is demonstrated in this type of case The outstanding characteristic is that no extrinsic allergen is proven to exist There are many mixed cases

Those primarily interested in dermatology and in rhinology have been rather slow to accept allergy as a factor of importance in their respective fields Hansel[54] has done much in recent years to broaden the appreciation of otolaryngological manifestations of allergy Dermatologists following the lead of Jadassohn and Bloch within the past few years have contributed much to our understanding of the skin manifestations of allergy in stressing the importance of contact allergy in the dermatoses There is still a tendency among dermatologists to minimize the possible importance of other allergenic factors such as food and inhalant allergens and to feel that contact allergy is a predominating element Sulzberger in particular among the dermatologists has emphasized the difference in type of skin lesions depending upon whether the causative allergen acts by contact or through the respiratory or gastrointestinal tract He has for example shown that an eczematous individual sensitive to silk may fail to give a positive patch test to this substance but may inhale the small amount of silk allergen that is present in dust in sufficient quantities so that it is carried through the circulation to the skin causing a consequent atopic dermatitis[55]

The patch test an important recent addition to allergic diagnostic facilities often will give positive reactions to substances which are quite negative by scratch or intracutaneously This is true especially of apparently non protein allergens such as soap heavy metals leather pollen oil cloths plastics chemicals drugs etc

An interesting sidelight on contact allergy in dermatology is the observation that individuals are not infrequently sensitive to constituents of ointments or other applications used to treat skin maladies This explains the statement not infrequently made by patients that the local remedies given by the physician made him worse rather than better Now with the application of the contact test the dermatologist may determine before beginning treatment which ointment base or other substance is appropriate for each particular patient

Passive transfer as developed by Prausnitz and Kustner, and elaborated in this country by Walzer represents a very distinct advance This will be discussed later

Testing and Interpretation

The limits of the present discussion preclude a detailed presentation of the technique of sensitization studies The following generalizations may, however, be found to be of help to those who would improve their technique in this field

Since it avoids the hazard of an unanticipated usually strongly positive reaction, the scratch method of testing should be employed before resorting to the intracutaneous method unless the intracutaneous test solution is so dilute that there is no possibility of a constitutional reaction In this case the latter possesses no advantage over the former and therefore need not be used

In the case of doubtful or negative scratch reactions there is still a possibility of sensitization and with the possible exception of the pollens, tests with the more important potential allergens should be repeated intracutaneously When this is done a concentration ten times weaker than scratch concentration will on the average give a ten times more sensitive reaction This is due to the fact that the intracutaneous method is roughly one hundred times more sensitive than the scratch Such concentration appears to be safe, provided preliminary scratch tests have been negative or no stronger than borderline

Allergens which actually cause trouble may give no stronger than borderline reactions The patient therefore should be instructed to watch carefully the effect of contact with such borderline reactors

Allergens to which the individual reacts very strongly, may fail to produce symptoms With relief of symptoms through avoidance or otherwise the patient then should try cautiously the result of contact with the different positively reacting substances He will find that he must continue to avoid some while others need not be prohibited

Etiology

Discarding any attempt at explanatory hypothesis, all that we can say concerning the etiology of clinical allergy is that for some incompletely understood reason certain individuals develop hypersensitiveness or idiosyncrasy to contact

with various foreign substances Probably the earliest known example in the history of mankind food idiosyncrasy was well known to the cave man It exists today among the lower animals We do not know why some persons are more likely to develop an idiosyncrasy than others There appears to be an hereditary factor following the Mendelian law The heavier the allergic incidence in one's progenitors the more likely is one to develop allergic symptoms Also the heavier the inheritance the more the likelihood of appearance of symptoms at an early age We do not know why one becomes sensitive to a particular food or other substance and not to others but there is evidence that one important factor especially among the major allergics is the degree or duration of exposure Evidently in a predisposed individual long continued heavy exposure is likely to produce sensitization but this statement must be qualified also inasmuch as one may have comparable heavy exposures to a number of potential allergens but become sensitized to only one of them

The number of possible substances against which one may become hypersensitive appears to be unlimited This was even true when in the past sensitization to proteins appeared to be an essential The number of chemically different proteins in the world appears almost limitless If in our present conception of the allergic state we add this idiosyncrasy to drugs and to apparently nonprotein contact allergens the enormous number of possible allergens becomes apparent One may even become hypersensitive to some new organic synthetic compound which has never previously existed in our environment Sulfonamides are an example Cases of urticaria agranulocytosis and other allergic manifestations were described in earliest reports of the value of sulfanilamide Roughly 15 per cent of those receiving these drugs become sensitized Penicillin sensitivity has been reported by Feinberg[36] Reaction sometimes follows the use of the drug to combat an infection and may take various forms rhinitis asthma urticaria or other manifestations of allergy

Among ingestant allergens we may safely say that one may become sensitive to any food We have just stated that the degree and frequency of exposure is a factor That this cannot be the only important factor is indicated in the preceding discussion in which we have seen that an outstanding characteristic in minor allergy and in experimental anaphylaxis is that the substance to which one becomes sensitive is one to which there has been little or no previous exposure or one to which the victim is exposed only occasionally This appears to be indeed the more important of the two factors We might modify our previous statement to say that if one does become sensitive to a substance to which he is chronically exposed this can be accomplished only as a result of prolonged and heavy exposure

The commoner inhalant allergens are the pollens house dust orris root feathers pyrethrum (a constituent of insect powders and sprays) animal epi

dermal inhalants, molds and silk The commoner contact allergens include soaps orris root pollen oils para phenylenediamine (ursol) the black dye used for dyeing cloths furs shoes, etc, therapeutic ointments and lotions, especially hair tonics and many occupational substances, with which the individual comes in close and prolonged contact In contact dermatitis the location of the eruption is likely to give an idea as to the etiology Occupational dermatoses are more likely to occur on exposed areas such as the face neck hands and arms Allergic dermatitis following the inhalation or ingestion of allergens is more likely to involve covered surfaces especially flexor surfaces It also often involves the face This is the so called neurodermatitis"

Among the commoner drug allergens we find quinine, ipecac, arsphenamine, barbiturates iodides aspirin, amidopyrine (pyramidon) sulfonamides and therapeutic sera

Physical allergy must be recognized also as a definite phenomenon Certain persons develop allergic symptoms from exposure to degrees of heat cold, sunlight and effort which are without effect upon the average individual The simplest but borderline example is the man who becomes intensely sunburned from no longer exposure than his friend who has at the same time developed little or no burn This is a borderline example, because the first person s reaction is but an exaggeration of a normal type of response He is hyperergic rather than allergic The person who on exposure to sunlight develops an entirely different condition such as urticaria is a better example

Most of the allergic manifestations particularly urticaria eczema vasomotor rhinitis and asthma do develop occasionally in individuals who appear to be unusually sensitive to the effects of heat cold sunlight and effort In the writer s experience physical allergy more often occurs in persons who are also sensitive to other substances and sometimes colors their reaction thereto A patient may be sensitive to some food or other allergen, with which contact occurs throughout the year but develop symptoms only in the summer, when hypersensitiveness to heat acts as an additional excitant

Pathological Physiology

The first response to entry of foreign allergen into the system appears to be a chemical or biochemical one, as yet incompletely understood which is explained best in terms of our present understanding of experimental anaphylaxis Accompanying and following this there are certain objective reactions which may be studied with greater facility These are smooth muscle spasm capillary dilatation serum transudation through the capillary walls catarrhal secretion of mucous glands and accumulation of eosinophils at the site of reaction These reactions may be very localized or quite widely disseminated

The location and preponderance of one or more of these reactions chiefly determine the resultant symptoms If a reaction becomes sufficiently widely disseminated (anaphylactic shock) there result pronounced fall in blood pressure prolongation of clotting time and a systemic leucopenia In extreme constitutional reaction or anaphylactic shock the reaction may be so explosive that the patient may be dead within five minutes following the allergenic contact

There is much that we do not know concerning the localization of allergic manifestations by predilection in different tissues of the body Obviously route of entry plays a governing part Inhalant allergens are more likely to produce respiratory symptoms hay fever and asthma Ingestant allergens are chiefly responsible for gastrointestinal allergy and internal manifestations such as migraine angioneurotic edema Meniere s disease and genitourinary symptoms Contact allergens usually produce dermal reactions

However in all of these there is at the same time a constitutional response Patch test with amidopyrine (pyramidon) in an individual predisposed to granulopenia may produce a severe fall in the total blood white count The inhalation of silk dust may cause eczema Food allergy may be responsible for eczema asthma or vasomotor rhinitis We may say therefore that route of entry determines the location of the response in many cases but there are undoubtedly other factors which often play a part

Certain tissues appear to be especially predisposed to react These are termed shock tissues and are such as contain relative preponderances of smooth muscle such as the bronchial tree the intestinal tract portions of the general vascular musculature the brain or more probably meningeal vessels possibly the peripheral vessels (thromboangiitis) and coronary circulation In the skin *the predominant reaction is more that of exudation and cellular infiltration The* part played by the liver is understood incompletely but perchance eventually *may be found to be an important one*

There is clinical evidence that sensitization need not be a general or constitutional *phenomenon but may be localized only in certain tissues of the body* An example is the person who always develops headache following the eating of Irish potato colitis after peaches and urticaria *from* chocolate This person manifests his allergy in three different ways but each of the three foods causes only one of the symptoms never either of the others

We must conclude therefore that in addition to portal of entry another possible factor is that of local sensitization in a shock tissue The chemistry of the allergen may be a factor also A woman sensitive by skin test to corn pollen but not to corn meal develops hay fever from the inhalation of corn pollen Following the eating of corn meal she experiences attacks of vasomotor rhinitis This might of course equally well be explained on the basis of local tissue sensitization

Non specific factors may play a part in localization A person sensitive to wheat sometimes may experience eczema following its ingestion, at other times colitis or vasomotor rhinitis or asthma occur The cutaneous symptoms in such a case were due to the action of a non specific factor mechanical irritation for example the rubbing of the collar on the back of the neck The non specific aggravating factor causing gastrointestinal symptoms was an unusually long period of constipation The localization in the respiratory tract accompanied a period of inhalation of large amounts of dust None of these non specific factors produced symptoms as long as the patient remained on a wheatless diet

Localized infection may act in the same way It has been shown that in a sensitized animal in which localized infection has been produced experimentally re injection of allergen is followed by an unusual concentration or mobilization of the allergen in the zone of infection This probably accounts for the occurrence of actual gall bladder attacks in individuals with gall bladder disease following the eating of foods to which they are allergic

The intensity of the allergic response may vary through all degrees from no apparent response to anaphylactic shock and death Some persons experience symptoms following every contact with a specific substance Others may establish contact often with apparent impunity, even though they are proven sensitive We speak of such sensitive persons as being in allergic equilibrium or in a balanced allergic state They are allergic but by some mechanism are able to maintain balance of normality in spite of contact This balance or equilibrium may be overthrown by an overdosage of the same allergen or by simultaneous exposure to two allergens neither of which alone will produce symptoms or by the interaction of any of a large number of non specific factors, some of which have been mentioned above

The part played by the sympathetic nervous system and by endocrine activities in coloring the allergic picture is indefinite at present so far as definite knowledge is concerned Adrenalin effect and the occasional improvement of patients following opotherapy indicate some factor There is also abundant evidence of vagotonia or better vago-sympathetic dystonia The writer is of the opinion that it will be found that these are factors which color or modify the functional pathology of the allergic response and may at times even determine localization but are not otherwise fundamental factors in the production of the allergic state

Symptomatology

We have termed allergy "the great intruder The pleomorphism of the symptomatology depends primarily on four factors, the nature of the allergen its route of entry the location of the shock tissue and the interaction of non specific factors Leaving out any discussion of allergy as a functional factor in

other clear cut disease complexes such as arthritis pneumonia malaria tuberculosis etc the symptomatology still is so variegated that it may be described best in terms of those disease complexes in which allergy usually or occasionally plays a dominant role The symptoms of each of these may be found elsewhere in the discussions of the particular diseases

Allergy usually plays a dominant role in asthma hay fever vasomotor rhinitis nasal polyps urticaria contact dermatitis neurodermatitis true migraine drug idiosyncrasy and the gastrointestinal manifestations of food idiosyncrasy The latter when acute are accompanied by nausea and vomiting sometimes followed by diarrhea and when subacute by colonic disturbances

Allergy sometimes may be the dominant factor in the following conditions herpes zoster seasonal conjunctivitis nasal stuffiness running or wet nose in children pruritus hiemalis hydroa aestivale erythema multiforme perianal eczema or pruritus ani purpura Meniere s disease acute diarrhea colic cyclic vomiting genitourinary symptom complexes periarteritis nodosa conjunctivitis keratoconjunctivitis neuroretinitis and edema of the optic disc

The allergic reaction may color the symptomatology of the following essentially non allergic diseases enuresis trichophytosis epilepsy peripheral neuritis mucous colitis spastic constipation dysmenorrhea possibly also angina and thromboangiitis obliterans Allergy may manifest itself sometimes as an allergic bronchitis or hoarseness without frank asthma or other clear cut allergic symptoms The symptom is chiefly a chronic cough sometimes with the raising of slight amounts of sputum This in the writer s experience when it does occur usually is due to food allergy

This is a long series of symptom complexes in which one must bear in mind the allergic possibilities The writer would emphasize however that in none of them must allergy necessarily be present Not all that wheezes is asthma If the wheezy child has aspirated a peanut it is more important to discover this than it is to do skin tests

The physician who is making an allergic study must at all times bear in mind that each case is one for differential diagnosis and that other possible etiological factors must be searched for with equal tenacity In this respect allergy is but one phase of internal medicine and in the diagnostic routine the two should never be divorced

Diagnosis

The allergic diagnosis commences with a careful history taking and painstaking physical examination together with whatever of the usual routine laboratory studies may be indicated Not until this general diagnostic survey has been made is one ready to make the special allergic studies

In the taking of the history it is indeed surprising how much information of an allergic nature may be obtained if one takes the pains to inquire into the minutiae of the past history This applies especially to food allergy but also to other forms After the sensitization studies have been made, and the list of positively reacting substances has been given to the patient, often he will recall many curious experiences with foods or other allergens to which he reacts which had been completely overlooked in the first discussion The history taking, therefore, may be divided into two parts the preliminary discussion and the follow up discussion after the completion of the sensitization studies

The questioning should in each case elicit any possible personal history of asthma hay fever frequent attacks of sneezing when in dust or certain localities or upon arising in the morning urticaria, eczema or other skin eruptions recurrent or periodic headaches and upsets of any nature whatsoever attributed to definite foods Food dislikes have been mentioned as correlated with food allergy, but the writer has been unable to find any parallelism between the two Indeed the frankly allergic usually remarks that he has been especially fond of one or more of the foods to which he is found sensitive The history should also develop the presence or absence of any of the above manifestations in the patient's family At the same time one should remember that allergy may be present in spite of the entire absence of a personal or family allergic history

Skin Testing — The scratch tests may be applied with dry powdered allergen moistened with one tenth normal sodium hydroxide or with a concentrated glycero-saline extract Scratches should be made with a dull pointed blade rather than a razor sharp one so as not to draw blood They should be made approximately one fourth inch long to ensure contact of the extract with the exposed epithelial cells Scratches are preferably made three quarters of an inch to an inch apart to prevent spread of the positive reaction to adjacent scratches They may be applied to any portion of the body although certain areas of the skin appear more reactive than others particularly the back and the abdomen As a rule the arms and back are used When the reaction may be unusually strong as in the case of pollens it is safer to use the arm since in the event of a constitutional reaction a tourniquet may be applied above the positive reaction thereby relieving the symptoms The softer tissues of the flexor surface are preferred The bend of the elbow is to be avoided since here the tissues are so flaccid that false positive reactions may appear The reaction is read at the end of 0 to 30 minutes Any degree of difference of a reaction from the general run of negatives in the same patient is to be recorded since borderline reactions may be obtained to substances which are actually responsible for symptoms

The intracutaneous test is applied with a 27 gauge needle and a tuberculin syringe the total amount of extract given intracutaneously being not more than 0 02 c c Otherwise false positive reactions appear from trauma With the

exception of bacterial vaccines no test substance should be used intracutaneously without preliminary scratch trial and none should be used that have been positive by scratch Under these circumstances a dilution about ten times weaker than that of the scratch appears safe The reaction may be at its height anywhere from 10 to 30 minutes after the test has been applied

To reduce the necessary number of needlings intracutaneous group extract are available for the foods grouped in accordance with their biological or genetical relationships Scratch tests should not be made with groups This introduces too much tendency to false negative reactions

Passive Transfer — The substance generated in the body which reacts with the antigen or allergen and which is termed reagin or antibody may be present only in certain tissues such as the skin or it may be present also in the circulating blood In the former case a positive skin reaction would indicate the possibility of skin manifestations following contact There would be no remote symptoms elsewhere in the body However if the reagin is present in the blood as well as in the skin allergenic contact may produce not only cutaneous symptoms but responses elsewhere in the body

If one is sensitive to wheat and reagins are only present in the skin the eating of wheat may cause urticaria or eczema If wheat reagins are present also in the blood wheat ingestion might cause urticaria, eczema migraine asthma colitis or even anaphylactic shock

A hay fever case may give positive skin reactions to two pollens such as timothy and ragweed and yet experience hay fever from inhaling one but not the other Reagins to the former are present both in the skin and the blood and presumably in the nasal mucosa Reagins to the latter exist only in this patient's skin The skin test to ragweed is positive but since this sensitization is localized and does not extend to the nasal mucous membranes no symptoms appear This localized sensitization in the skin alone explains many of the so-called false positive reactions reactions to foods pollens etc which do not actually give the patient trouble

If a patient with pneumonia requires serum treatment he is first tested with horse serum by skin test A positive reaction is interpreted as indicating allergy thereto In this case serum is not given or else the patient is given rapid preliminary desensitization As a matter of fact a positive skin reaction does not always indicate that such an individual will necessarily have allergic shock following serum administration Reagins present in the skin and responsible for the positive reaction may not be present in the blood If this is actually the case one could give anti pneumococcic serum without risk But since we usually do not know whether there are reagins in the blood and since serum administration in penumonia diphtheria tetanus etc usually is urgent it is safest to desensitize if the skin test is positive

In the taking of the history it is indeed surprising how much information of an allergic nature may be obtained if one takes the pains to inquire into the minutiae of the past history. This applies especially to food allergy but also to other forms. After the sensitization studies have been made and the list of positively reacting substances has been given to the patient, often he will recall many curious experiences with foods or other allergens to which he reacts which had been completely overlooked in the first discussion. The history taking, therefore may be divided into two parts the preliminary discussion and the follow up discussion after the completion of the sensitization studies.

The questioning should in each case elicit any possible personal history of asthma, hay fever, frequent attacks of sneezing when in dust or certain localities or upon arising in the morning, urticaria, eczema or other skin eruptions, recurrent or periodic headaches and upsets of any nature whatsoever attributed to definite foods. Food dislikes have been mentioned as correlated with food allergy, but the writer has been unable to find any parallelism between the two. Indeed the frankly allergic usually remarks that he has been especially fond of one or more of the foods to which he is found sensitive. The history should also develop the presence or absence of any of the above manifestations in the patient's family. At the same time one should remember that allergy may be present in spite of the entire absence of a personal or family allergic history.

Skin Testing — The scratch tests may be applied with dry powdered allergen moistened with one tenth normal sodium hydroxide or with a concentrated glycero-saline extract. Scratches should be made with a dull pointed blade rather than a razor sharp one so as not to draw blood. They should be made approximately one fourth inch long to ensure contact of the extract with the exposed epithelial cells. Scratches are preferably made three quarters of an inch to an inch apart to prevent spread of the positive reaction to adjacent scratches. They may be applied to any portion of the body although certain areas of the skin appear *more reactive than others* particularly the back and the abdomen. As a rule the arms and back are used. When the reaction may be unusually strong as in the case of pollens it is safer to use the arm since in the event of a constitutional reaction a tourniquet may be applied above the positive reaction thereby relieving the symptoms. The softer tissues of the flexor surface are preferred. The bend of the elbow is to be avoided since here the tissues are so flaccid that false positive reactions may appear. The reaction is read at the end of 0 to 30 minutes. Any degree of difference of a reaction from the general run of negatives in the same patient is to be recorded, since borderline reactions may be obtained to substances which are actually responsible for symptoms.

The intracutaneous test is applied with a 27 gauge needle and a tuberculin syringe the total amount of extract given intracutaneously being not more than 0.0 c c. Otherwise false positive reactions appear from trauma. With the

small amounts into the conjunctival sac It is washed out with physiological saline after 3 minutes and the reaction is read after another 5 or more minutes This consists of congestion and redness of the conjunctiva is compared with that of the other eye The reaction may be controlled promptly after the reading with dilute adrenalin solution (1 to 5 000) This reaction tends to eliminate false positive as well as false negative reactions The skin may be sensitive to a pollen while the mucous membranes are not and vice versa

Bacterial Tests —There is still abundant divergence of opinion as to the specificity of bacterial allergy An occasional case gives positive skin reactions to a particular pure culture vaccine and responds satisfactorily to desensitization therapy therewith In the majority a definite allergic bacterial etiology is not demonstrated However in the occasional case just mentioned results of treat ment are sufficiently good while in others results with bacterial vaccines are good in spite of negative sensitization reactions For this reason in cases in which results otherwise have been unsatisfactory bacterial studies are worth while The vaccines by preference should be autogenous and isolated in pure culture They are made in the usual way and are tested intracutaneously in *volume of 0 01 to 0 02 c c Rarely a positive reaction with wheal and flare is* observed within half an hour More frequently the positive reaction is manifested by the tuberculin type of delayed pseudo-inflammatory reaction after 24 hours This is also true of the mold extracts such as trichophytin and oidiomycin

Prognosis

Allergy is essentially a chronic state in the treatment of which relief rather than cure should be the objective It is true that one may entirely lose one s sensitization which is tantamount to cure but the tendency to develop new sensitizations to additional substances persists in which case symptoms recur and the new offender must be discovered and controlled

From Vaughan s experience with treatment properly administered satisfactory relief is obtained as follows in seasonal hay fever from 90 to 100 per cent relief occurs in two thirds of cases 75 per cent relief or better in four fifths in perennial asthma and vasomotor rhinitis due to extrinsic causes 80 per cent in respiratory allergy due to intrinsic causes 25 to 45 per cent migraine and allergic dermatitis and colitis about 50 per cent urticaria and angioneurotic edema 75 per cent

There are three cardinal principles of allergic therapy

1 Treat the patient as a whole in the broader medical sense One is not attempting to treat allergy rather a patient with allergy The allergic treatment of a patient with a concomitant tuberculosis is altogether different

Obviously it is sometimes desirable to know whether reagin is present in the blood This is often true in respiratory allergy, migraine abdominal allergy and in all cases in which there is a question as to whether a positively reacting substance actually is responsible for trouble To determine the presence of blood reagins the Prausnitz Kustner reaction is utilized Serum or plasma is obtained from the patient and injected intracutaneously into the skin of a non allergic recipient A rather large amount, from 0 07 to 0 1 c c, is given in each test area This passively sensitizes the non allergic recipient in a zone of about one half inch diameter around the point of intracutaneous administration After 48 hours this sensitized area representing the patient, is tested intracutaneously with 0 02 c c of the allergen extract under suspicion As a control the same amount is introduced into a non sensitized area of the recipient s skin If the sensitized reaction is stronger than the control reaction, the patient from whom the blood was obtained has reagins in his blood against this particular allergen

In this way many of the false positive skin reactions may be eliminated The test is used also in infants whose skin is relatively nonreactive and in individuals with extensive dermatitis or dermographic skin, on whom skin tests are impracticable

The Patch Test — This is applied in cases of contact dermatitis As a rule there are no reagins in the blood against substances giving positive patch tests Indeed the scratch and intracutaneous tests usually are negative to positive patch reactors The reverse usually is true also although occasionally exceptions are seen as in the case of orris root which may be positive both by patch and by cutaneous or intracutaneous test

Any substance not naturally irritating coming under suspicion as a possible environmental factor may be used for the patch test Contact allergens are not limited to proteins A small amount of the natural substance slightly moistened if necessary is applied to a non irritated skin area, covered with a square of cellophane or wax paper about one inch square and this in turn is covered with a strip of adhesive A control square of cellophane or paper is applied also A positive reaction read after 1 to 7 days depending upon the degree of sensitivity, is manifested by a square of dermatitis corresponding to the square of cellophane or paper and resembling the original skin lesion of which the patient complains Many persons are sensitive to adhesive plaster In this case the cellophane may be applied with a special non allergenic collodion prepared by Johnson and Johnson or with a ring of rubber cement

The Ophthalmo Reaction — The conjunctival test is used with inhalant allergens more especially pollens when the skin test gives uncertain readings If in the absence of a positive skin reaction one is still of the opinion that a certain pollen may be responsible for symptoms this dry pollen may be introduced in

hemotherapy helps temporarily in a small proportion of cases and may be tried when other specific measures have failed

Histamine used in the treatment of certain allergic manifestations has given favorable results in the hands of some workers especially Horton The use of histamine azoprotein has given less encouraging results

Sensitization and Desensitization

Factors Influencing the Development of Sensitization

(1) One may become sensitized to foreign serum even though one does not develop serum sickness after the first injection The absence of serum sickness does not indicate that the person has not become sensitized

(2) Children from allergic families have been found more likely to become sensitized than children from nonallergic families History of allergy therefore becomes important

(3) The site of injection plays a part One is less likely to become sensitized after hypodermic than after intraspinal or especially intravenous injection This is reflected also in the severity of reactions in those who are sensitized Park[57] reported 1 death per 50 000 serum injections given almost entirely subcutaneously Bullowa estimated anaphylactic death at 1 in 700 following intravenous injection[58]

(4) The quantity of serum administered is important About 10 per cent of those who receive 10 c c of horse serum intravenously become sensitized while 90 per cent of those receiving 100 c c do so

(5) Hapten combinations of serum with other substances especially toxins appear to increase the tendency to sensitization Cordon and Creswell[59] found that 74 per cent of children receiving serum who had had previous injections of diphtheria toxin antitoxin developed serum disease as contrasted with 43 per cent of those who had had horse serum previously but no toxin and 16 per cent of those receiving serum for the first time

(6) The nature of the serum itself plays a part The more highly refined serum globulin is less likely to produce sensitization than is whole serum

(7) The animal itself plays a part Some horse sera are more highly antigenic than others Park[60] tested a series of horse asthmatics with the sera of three different horses Ten per cent reacted to the serum from the first horse 35 per cent to the second and 60 per cent to the third

from the allergic treatment of one with concomitant duodenal ulcer In this respect allergy must not be divorced from the broader field of internal medicine

2 When allergen avoidance is practicable this method should be employed in preference to desensitization There is a natural tendency toward recovery toward loss of specific sensitization provided contact with the specific allergen is avoided for a sufficiently long period The necessary interval of avoidance to accomplish loss of sensitization varies from a few months to many years In a series of allergic migraines the writer found the average period about four and one half years

3 When avoidance is impractical desensitization must be employed This usually is the case with substances such as pollens housedust occupational dusts and bacteria It is rarely the case with any food When desensitization is carried out it should not be done in a haphazard manner but with a clear understanding of the objectives to be gained

Preseasonal pollen treatment requires building up prior to the season to a sufficiently high top dose so that the patient can tolerate exposure to any amount of pollen with which he will naturally come in contact in the air For best results a top dose of 20 000 pollen units or 1 c c of - per cent extract is most desirable This appears to be as true on the Atlantic seaboard as in the Mississippi Valley where ragweed concentration is much higher Probably this is because on the Atlantic seaboard only the extremely sensitive develop symptoms and these are comparable not to the general run of mid western cases but to the extremely sensitive With the trees and grasses a top dose of 5 000 or 10 000 pollen units usually is sufficient since grass and tree pollen concentration in the air is far lower than that of the ragweeds

Coseasonal treatment requires frequent small doses rarely higher than 100 pollen units Attempts to increase the dosage farther often overthrow the allergic equilibrium making symptoms worse

The perennial case sensitive to dust and the like should be treated as a coseasonal case in which the season lasts through the year Frequent small doses in this case once or twice weekly usually suffice Treatment must be continued for many months In the event of return of symptoms in spite of treatment there is still leeway for increases in dosage but as long as the patient is relieved with small doses there seems no logic for increasing them beyond that giving relief especially in view of the fact that in either case treatment must be long continued

The same principle applies in bacterial desensitization If as is usually the case the causative bacterium cannot be eliminated small desensitizing doses are preferable to large immunizing doses

Non specific desensitization ' with substances such as peptone and auto

of tests is so simple and can be done with such little delay that it must be preferred The test should be made when the history is suggestive or better routinely Certainly the eye test should be done routinely

There have been a few reports of deaths after a first intravenous injection of therapeutic serum in persons with no allergic history and with negative skin and eye tests The cause in these is unknown

Prevention of Serum Accidents

If the patient is allergic to horse serum and the need for therapeutic serum is unquestioned a substitute serum (bovine rabbit goat or sheep) should be used if available Preliminary testing should be done with the substitute serum

The following general rules formulated by Coca[61] are helpful (1) If there is a history of horse asthma or nasal allergy and the skin test and eye test are positive the patient should not receive horse serum although there is a remote possibility of successful desensitization (2) If the history is positive but skin test and eye test are negative serum may be given very cautiously A horse asthmatic with negative skin and eye tests probably is allergic to horse dander but not to horse serum (3) If there is a negative history but the skin and eye tests are positive it is not safe to go ahead without careful desensitization This is often the situation in cases who have had horse serum in the past

Desensitization

Persons who have become sensitized to horse serum from previous injection often can be desensitized Horse asthmatics who react to horse serum usually are so highly sensitized that desensitization cannot be accomplished although it may be tried cautiously[6]

In outlining a program for desensitization one must remember certain cardinal experiences (1) one drop of undiluted serum given intravenously has killed (2) 0 05 c c undiluted endermally has done likewise (3) most of the serious reactions from intravenous injection have occurred with administration of the first 10 c c (4) many of the accidents have happened at the time of change from preliminary subcutaneous to direct intravenous administration

A program of therapy should take the above points into consideration The initial dose must be way below one drop of undiluted serum intravenously or 0 05 c c endermally Reactions at the time of the change from subcutaneous to intravenous desensitization are due to the fact that not all of the subcutaneously administered serum enters the circulation at once Fifteen to twenty four hours may be required for all to be absorbed There should therefore be a radical drop in dosage when the change to intravenous injection is made Finally if

Prevention of Sensitization

Although one cannot prevent serum sensitization there are steps which one can take to lessen its frequency The first and most obvious is not to give serum unless its need is clearly indicated For those diseases in which serum therapy has not been proved superior to other measures, the latter should be used first Fortunately sulfonamides and penicillin intravenously, intramuscularly, locally and by mouth have to a great extent supplanted serums in the treatment of many virulent infections

Tetanus and diphtheria toxoids containing no serum mark a great advance It has heretofore been a regrettable necessity that in immunizing children against diphtheria and tetanus we have made it difficult or hazardous for them to be given a needed therapeutic measure later

Recognition of Sensitization

Proof of sensitization after careful questioning concerning personal and family allergic history and previous serum injections is based on quite reliable objective tests The importance of family history is illustrated in the tragedy of a physician who wished to immunize his two daughters who had been exposed to diphtheria One had had recurrent urticaria He gave the prophylactic injection of antitoxin to the other who had no allergic history She promptly died Although these girls were twins the same might occur with less closely related siblings

Recognition of sensitization is so simple that is should not be neglected One marvels at the temerity with which surgeons repeatedly inject tetanus antitoxin without untoward results This is an indication of the relative rarity of severe reaction but it is scarcely an adequate excuse for an anaphylactic death occurring without the preliminary use of adequate safeguards A series of 999 negative tests is justified if it saves the life of the thousandth case

Objective tests consist of preliminary scratch, conjunctival and endermal tests with horse serum Although the therapeutic serum may be used natural horse serum is preferable since the former occasionally tends to give false positive reactions The serum is best diluted 10 times If the scratch test is negative after 21 minutes a drop of $\frac{1}{10}$ serum is placed in the conjunctival sac If at the end of 5 or more minutes there is no conjunctival injection especially in the lower sac, an intracutaneous test is made using 0 02 c c of $\frac{1}{10}$ dilution If this is negative at the end of 15 or 20 minutes one may proceed with therapy This series of tests progresses from the least sensitive but safest scratch test through the intermediate eye test to the most sensitive endermal test Many physicians use the eye test alone This probably is adequate for nearly every case, but the series

in contradistinction to other clinical conditions which might be confused with an allergic problem

One cannot overemphasize the importance of consultations with physicians in other specialties to rule out an allergic or non allergic factor in the problem

The allergy diagnostic study must be complete including not only routine scratch and intracutaneous tests but also other special allergy tests The evaluation of results from such a detailed investigation can only be made after considering the history the reports of the tests and other clinical findings Further management has to be based upon the allergist s experience

The patient has to be considered and treated as a whole along with his allergy management coincidental diseases or physical states should be handled adequately

Thus the effective therapeutic program should encompass dietary restrictions avoidance of the offending inhalant and contact substances hyposensitization in selected instances consultation with otolaryngologists dermatologists or other specialists if necessary and recognition and control of emotional and physical states

Allergy is now being appreciated and its development has passed the embryonic stage It is imperative that the clinician be cognizant of and consider in the handling of his varied problems possible allergic factors The point to remain uppermost in the clinician s mind as far as allergy is concerned is to think of it recognize it and give allergy its just consideration

a person allergic to horse serum has taken 10 c c of undiluted serum or its equivalent in diluted serum intravenously without reaction one may then give the remainder reasonably rapidly

The following program is satisfactory For moderate sensitization as indicated by the skin and eye test, serum is diluted 1 to 10 For the more highly allergic individual it is diluted 1 to 100 Usually 1 to 10 is satisfactory Injections are given subcutaneously in an extremity every 20 or 30 minutes, commencing with 0 01 c c The dose is doubled each time although with the higher dosages the increase may be reduced to 50 per cent After 1 c c of 1 to 10 serum has been given the same schedule is repeated with undiluted serum starting with 0 1 c c Injections are given into the extremities so that if a reaction does occur a tourniquet may be applied above the site of the injection to reduce absorption into the circulation If possible just one or two extremities are used Further discussion of the control of reactions is found in Chapter VI B With undiluted serum the subcutaneous dose is increased as described until a total of 10 c c (*not* a *final* dose of 10 c c) has been given If there has been no serious reaction the remainder of the total desired dose if any may be given without further delay

This procedure requires about 3 hours, but the time may be extended by several hours if the patient develops systemic reactions during the course of treatment After such reactions have occurred and been controlled, it is well to repeat the last dose or even to start with the next to the last preceding dose

The program for intravenous injection is somewhat different Preliminary desensitizing injections may be given subcutaneously according to the same schedule up to 10 c c of undiluted serum After this the schedule is repeated intravenously starting again with 1 to 10 dilution the initial dose being 0 1 c c After a total of 10 c c has been given intravenously without serious reaction, the entire remaining amount may be given slowly

An alternative procedure is to give the serum intravenously from the start beginning with 1 to 1 000 or 1 to 10 000 dilution, which is introduced by continuous venoclysis at the rate of 100 c c per hour if no serious reaction occurs Starting with 1 to 10 000 dilution one may at the end of an hour change to 1 to 1 000 then 1 to 100 1 to 10 and finally undiluted serum The total amount is administered over such a long period that one has ample time to control reactions

Conclusions

In the investigation of allergic individuals there are many points of major significance Complete and comprehensive historical investigation as well as physical examination including both routine and special laboratory studies enables the clinician to determine whether the patient has a frank allergy problem

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CHAPTER VI-B

SERUM SICKNESS

By FREDERICK R. TAYLOR

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Clinical allergy in general and the fundamental principles of allergy have been discussed already by Vaughan (Vol II Chapt VI-A) and Walker (Vol II Chapts VII and VIII) in this work so the present discussion will deal only with serum sickness and accidents and similar phenomena following the use of vaccines bacterins etc

Definition —Serum sickness may be defined broadly as the untoward clinical manifestations following the administration of prophylactic or therapeutic sera Occasionally similar manifestations have followed the use of certain other biologic products such as vaccines and bacterins

HISTORY

The first mention of serum sickness which the author has found in the literature is in a symposium on infectious and toxic erythemas in general presented to the Medical Society of the Hospitals of Paris in 1894 by LeGendre Siredey Rendu Burlureaux Catrin and Hayem[1] who discussed among other things certain eruptions following the use of diph

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tracheotomy The interested student is referred to their work for this remarkable description In this same discussion Thompson cited a case of horse asthma In 1909 Besredka[8] discussed the prophylaxis of serum disease and advised warming serum to 56° C before injection he also described a technic for desensitization by the repeated injections of minute amounts of serum

In 1897 Engelmann[9] noted the association of neurological disturbances with serum injections as did Grunberger[10] in 1904 and Cangolphe[11] in 1908 These authors however did not make clear any etiologic relationship between the serum and the syndrome According to Allen[7] Thaon[12] was the first to recognize this in 1910 but his publication attracted little notice Since that time numerous reports have appeared in the French literature and a few from other parts of Europe and from North and South America It is interesting to note the increasing frequency of these reports in the past seven years (1931–1937) despite the increasing refinement and concentration of medicinal sera According to Young[14] Petit[15] published the most exhaustive treatise on the neurologic manifestations of serum disease in 1925 In 1933 Demme[16] noted the rarity of such manifestations in Germany in contrast to their frequency in France In recent years the literature of serum disease in general has become enormous

ETIOLOGY AND PATHOGENESIS

For a discussion of the fundamental principles of these phases of our subject the reader is referred to the chapters on clinical allergy bronchial asthma and hay fever in this volume Suffice it to say here that serum sickness is due to a congenital or acquired sensitivity to the foreign protein in the serum or other biologic product which gives rise to it Sensitiveness to serum depends in part on the species of animal from which the serum is obtained Thus a patient sensitive to horse serum may be quite insensitive to goat serum Moreover the serum of certain individual animals seems to cause more severe reactions than does that of other animals of the same species (personal communication from Dr John H Hamilton Director of the North Carolina State Laboratory of Hygiene) The reason for this is not clear While apparently any horse serum may cause neurological complications for some unknown reason antitetanic serum unquestionably is the chief offender this may possibly be due to the tremendous number that receive prophylactic antitetanic serum injections Even small prophylactic doses of 1500 units seem to cause about as much trouble as massive therapeutic doses of any serum

theria antitoxin Burlureaux was the first to mention this topic and cited a case To this report LeGendre added the statement that the existence of various eruptions some days after the subcutaneous injection of antidiphtheric serum was so frequent in his experience that he thought it always well to warn the family of the possibility of cutaneous manifestations He also noted the great variability in the characteristics of the eruption and of the time interval between the serum injection and its appearance stating that it might appear as long as 20 days after injection He also described the fever articular and periarticular pains nausea vomiting cerebral excitement or depression phosphaturia and urobilinuria and expressed the opinion that the symptoms were due to the serum of certain horses rather than to the antitoxin

The Germans seem to have adopted a rather conservative attitude regarding untoward symptoms following serum injections Eulenberg in 1896 protested against the term serum poisoning' used by Baumler at a meeting of the Congress of Internal Medicine Paltauf[3] in the same year noting fatal cases objected to blaming the deaths on the antitoxin and advanced the modern idea that they were due to a peculiar condition of the patient According to Goodall[4] one of the earliest deaths reported was that of a child of Professor Langerhans following a prophylactic dose of antidiphtheric serum

The first reference to serum sickness in the American literature which the author has found is in an article by Cumston in 1897 in the Boston Medical and Surgical Journal He noted abscesses at the site of injection and cited epidemics of such abscesses and also exanthemata arthropathies albuminuria urobilinuria peptonuria epistaxis metrorrhagia vomiting diarrhea lymphadenitis splenic enlargement edema of the extremities cardiac disturbances such as arrhythmia tachycardia and gallop rhythm and also death He made the statement that the only serum never known to cause complications when injected into man is human serum He also recognized that the serum rather than the antitoxin caused the reactions

In 1903 Arthus reported the phenomenon usually known by his name of induced local tissue sensitization in guinea pigs so that gangrene would develop at the site of a subsequent injection of serum In 1908 Schmitt White and Thompson[7] discussed serum sickness and Schmitt gave a classic description of his own symptoms in a very severe attack of serum sickness which exhibited an extraordinary range of phenomena including uncontrollable sneezing pain in the eyes nose and throat dyspnea dysphagia urticaria swelling of the tongue and extremities and a truly alarming edema of the glottis so that preparations were made for immediate

branes is frequent In anaphylactic shock edema of the bronchial mucosa probably plays a very important part though bronchiolar spasm also is considered a factor by most authorities Fluid effusions into the joints are common Any part of the nervous system central or peripheral also may be involved as may any region of the gastrointestinal tract Edema of the larynx is a dreaded complication Practically any organ or tissue of the body may be involved The temporary anuria which has been reported may be due to renal edema Circulatory collapse is chiefly vasomotor in nature Chalier and Thiers[22] find the alkali reserve lowered in serum disease Ratner believes that all who show anaphylactic shock on a first injection of horse serum have been sensitized previously to horse dander a hypothesis the writer finds difficult to accept in this automobilious age Regarding the neurological manifestations of serum disease some writers have suggested the possibility of a dual effect from direct toxicity to nerve cells or their processes and from urticarial wheals or edema in the nerves or perineural structures causing pressure phenomena but the weight of opinion today favors the latter factor as the more important if not the sole one This view is supported strongly by those cases in which the pains and paralyses are intermittent suggesting pressure from fugacious recurring wheals or edematous areas as in a case observed by the author Roger Mattei and Paillas[23] believe a meningoradiculitis to have been the essential pathological condition in the cases studied by them Dechaume and Croizat[1] in experimental chronic anaphylaxis in rabbits found both hemorrhagic and nonhemorrhagic lesions in the nervous system The hemorrhagic lesions were of two types (1) localized hemorrhages confined to the perivascular sheaths and (2) hemorrhages infiltrating the neighboring parenchyma The nonhemorrhagic lesions consisted of small scattered areas of encephalomalacia

Symptomatology

The symptoms may be classified in two ways as (1) local or general and (2) immediate or delayed The local symptoms apply particularly to subcutaneous or intramuscular injections and usually are negligible with intravenous administration

Immediate Local Symptoms

Beside moderate discomfort at the site of injection an erythematous and slightly swollen area may appear around the puncture wound within a few minutes and last for a few hours In addition the writer has noted

Mignot[17] states that the size of the dose is of no significance with regard to neurological complications Gordon[18] reporting two cases of neurological symptoms due to prophylactic scarlet fever antitoxin takes the rather extreme position of suggesting that a patient before having any serum administered should be required to sign a statement relieving the physician from the consequences thereof This probably would cost many lives through creating an excessive fear of the most indispensable therapeutic and prophylactic sera and would seem to be a mistaken policy except in unusual cases

Besides tetanus and scarlet fever antisera reports of neurological phenomena due to many others have appeared including pneumococcus meningococcus diphtheria dysentery a serum given for tuberculosis (Young)[14] etc In addition to these similar phenomena have occurred following the use of typhoid and staphylococcus bacterins The paralyses following antirabic virus are well known and encephalitis is a very rare complication of smallpox vaccination (Vol VI Chapt III–A) As these last two are living viruses the pathogenesis may be different in some instances at least from that of serum sickness as it is conceivable that they might give rise to actual infectious processes in the nervous system However some recent unpublished work of Harold M Horack suggests very strongly that most if not all of the untoward reactions to antirabic vaccine are allergic in nature and appear in those who have shown previously evidences of allergic susceptibility

Leahy[19] cites a remarkable case of sudden death seven days after the administration of a dose of cold vaccine Foster Kennedy[20] sums up the whole situation well when he remarks When all is said and done these are rare accidents and but a small price to pay for the inestimable benefits obtained by serum therapy in general

Coca[1] points out that the ordinary serum sickness differs from other forms of human hypersensitiveness in having a definite incubation period in its occurrence in a high percentage of those exposed to it and in the lack of any special age incidence He also notes that the American Indian is much less subject to all forms of allergic disturbance than is the Caucasian

Pathology

The essential pathology of serum sickness is an acute edema associated with an increase of capillary permeability and a varying degree of vasomotor paresis due to the presence of the irritating protein In the skin this manifests itself by the varying eruptions Edema of the mucous mem

Delayed General Symptoms

The vast majority of cases of serum sickness come under this heading and the ordinary type of serum sickness is in this class Many authorities limit the term serum sickness to this group of cases and call the cases with immediate general symptoms serum accidents or anaphylactic shock

Skin and Subcutaneous Tissues — The commonest delayed general symptom is a general eruption which may be erythematous urticarial papular or one or more of a great variety of types including in rare cases hemorrhagic manifestations such as purpura Different types of eruption may appear in the same patient in the same attack Often the eruption is most intense at the site of injection and may appear there first soon spreading all over the body Statistics from different observers show an incidence of an eruption in from 10 to 60 per cent of patients given serum It is generally accepted that other things being equal the smaller the bulk of the serum injected and the greater the degree of its purification and refinement as e g in the highly refined serum globulin preparations the less will be the incidence of serum sickness Swelling of the eyelids lips face or extremities like that seen in angioneurotic edema is not infrequent Freitag[76] has reported a case with universal subcutaneous edema lasting two days

Joints and Periarticular Structures — Pains in and around the joints frequently accompany the eruption They vary from mild to agonizing Swelling of the joints and periarticular structures may or may not be evident Extensive effusions of fluid occur occasionally According to Boots and Swift[77] when the joints are involved it is a true arthritis and fluid aspirated from such joints is indistinguishable microscopically from that obtained from joints affected by rheumatic fever Veillet[78] has reported a peculiar case in which the synovial membranes and tendon sheaths in all four extremities were affected without true joint involvement A pale swelling was noted in the region of the parts involved

Fever of slight to moderate degree may be present or absent *General malaise* is the rule *Chills* may occur

Gastrointestinal Tract — Anorexia nausea and vomiting are not uncommon Much less frequent are diarrhea and abdominal cramps The tongue may be swollen grotesquely Chevalier Jackson[79] reports a unique case showing great swelling of the tongue with totally obstructive edema of the wall of the esophagus without laryngeal or tracheal involvement or respiratory embarrassment

Respiratory Tract — Intractable sneezing has been reported and epis-

frequently especially in children intermittent local muscle spasms that may waken them suddenly during the night after the injection They rarely persist longer than one night

Immediate General Symptoms

These offer the most serious problems which arise in serum sickness and nearly all the deaths are associated with them They appear with dramatic suddenness and may overwhelm the patient in a few minutes These symptoms are grouped together under the term anaphylactic shock Within a very few minutes after injection the patient may turn pale and become extremely dyspneic or even show a sudden complete arrest of respiration Cyanosis develops rapidly With dyspnea there may be a pouring out of frothy serum from the nose and mouth and the patient may drown in his own secretions The writer saw one case in which respiration stopped within less than three minutes after a prophylactic intramuscular injection of antitetanic serum the child appearing as if dead with widely dilated pupils though fortunately normal breathing was reestablished after artificial respiration and epinephrin had been employed and the boy survived Lewis believes that in these cases of very rapid development of grave symptoms from supposed intrasmuscular injections there must have been an accidental intravenous injection stating that serum injected intramuscularly is absorbed slowly through the lymphatics Be that as it may there are many cases on record of anaphylactic shock in which the reports give no hint of the suspicion of such an accident A general urticarial eruption may or may not accompany the shock Goodall[4] mentions muscle twitchings convulsions and hyperpyrexia as rare accompaniments Chills are frequent after intravenous injections but usually are independent of shock and should cause no alarm

Delayed Local Symptoms

Some of these are intimately bound up with the delayed general symptoms and will be discussed in connection with them There is however a special type of delayed local reaction fortunately rare which practically never occurs in patients who have not had a previous injection of serum This is comparable to the Arthus phenomenon in guinea pigs It consists of the appearance of a hard indurated area at the site of injection some days later which spreads until a large dense mass is formed This may be absorbed slowly but in extreme cases goes on to necrosis and the mass eventually sloughs out with extensive scarring

and accommodation The conjunctive remained normal for 15 to 30 minutes after injection and then became congested and remained so throughout the febrile period There was profuse lacrimation in 6 of the 10 including all 4 with dilated pupils

The fundi of the 75 cases showed varying effects In some no reaction could be detected In others the reaction was moderate in still others intense In the cases with an average febrile reaction 100° to 101 F there was no change in the fundi for the first half hour In one to one and a half hours there was a diffuse hyperemia with dilatation of the retinal vessels and slight elevation of the disc cup Definite papilledema was noted in 20 per cent of the cases and 10 per cent of the patients noted definitely blurred vision Similar reactions occurred later in the delayed urticarial stage There was no permanent impairment of vision and no true optic neuritis Mason[33] however has reported definite optic neuritis requiring four months to clear up In his case the spinal fluid was clear but under increased pressure

Ears — The external ears may be involved along with the rest of the skin and subcutaneous tissues In 1936 Cutter[39] gave the first report of a case of involvement of the auditory nerve in serum sickness

Nervous System Symptoms

Involvement of the nervous system while relatively infrequent is of no little importance for it may cause prolonged suffering and disability and may give rise to errors in diagnosis The writer once erroneously diagnosed a condition as progressive spinal muscular atrophy that turned out to be a neurological type of serum sickness and ended in complete recovery American text books of internal medicine have largely ignored the neurological manifestations of serum sickness despite their clinical importance so the writer wishes to emphasize them These manifestations are varied The cases fall into two main groups the *peripheral* and *central* according to the site of the lesions

The *peripheral nervous symptoms* are more frequent and may be subdivided as follows the radicular type the mononeuritic type and the polyneuritic type

Radicular Type — This is the commonest form of all and includes the classic neurological type Nerve roots are involved usually motor and sensory though either may be affected alone with the usual radicular distribution of symptoms and signs The involvement may be unilateral or bilateral more often the latter though the symptoms rarely are equally well marked on the two sides The classic type affects the upper ex

taxis noted Laryngeal or tracheal edema may develop and threaten life Bronchial and pulmonary edema are more likely to occur as part of an immediate anaphylactic shock than as delayed phenomena

Circulatory Tract — Syncope usually with profuse sweating and cold extremities has been described as a delayed symptom by a number of observers including Crooks[30] Dudgeon[31] and others Crooks[30] has reported tachycardia with a dilated heart lasting a week Lavergne Morel and Jochum[3] cite a case of transient Stokes Adams syndrome developing during serum sickness in convalescence from facial erysipelas Various arrhythmias and gallop rhythm have been noted

Blood — The blood findings are inconstant though leukocytosis is the rule The white cell count has been reported as high as 50 000 per cu mm but this is unusual Eosinophilia may or may not be present Bouche and Hustin[33] state that there is a decrease in blood coagulability and an increase in the refractive index of the patient s serum

Lymphatic System — A generalized nonsuppurative adenitis is by no means unusual in serum sickness this usually is accompanied by fever but the fever tends to subside in a few days whereas the adenopathy usually takes some weeks to clear up Enlargement of the spleen has been noted in a number of cases

Urogenital System — Anuria is not uncommon for a day or two but is benign and urinary secretion is reestablished soon Polyuria is noted occasionally Albuminuria is very common and may be accompanied by hyaline and epithelial casts These phenomena too are transitory Transient hematuria has been reported Phosphaturia urobilinuria glycosuria and the appearance of various other temporary abnormalities in the urine are not infrequent but are of no ill omen Painful tender swollen testicles have been reported by Goodall[4] and by Carrieu[34] and Goodall has noted also edema of the scrotum and penis The testicles returned to normal within less than a week

Endocrine System — According to Kraus and Chaney[35] Cordier Morenas and Delore[36] have reported a case of grave adrenal involvement in serum sickness beginning ten days after serum was injected exhibiting the clinical picture of Addison s disease and lasting four months

Eyes — Brown[36] has published a record of the ocular symptoms in 75 patients with reactions following the intravenous administration of serum In 10 of these patients no mydriatic was employed in order to observe the pupillary changes In the other 65 the eyes were examined under homatropine before the serum injection and at frequent intervals thereafter In 4 of the 10 patients examined without the mydriatic the pupils dilated regularly and equally and were sluggish in their reactions to light

While the neurological phenomena usually are preceded or accompanied by ordinary serum sickness (uticaria arthralgia etc) this is not necessarily so as they have been observed in the absence of the more usual syndrome

Diagnosis

Ordinarily this is obvious In neurological cases the acute onset after the injection of a serum or vaccine should put the observer on his guard against diagnosing such conditions as progressive muscular atrophy amyotrophic lateral sclerosis etc If the injection of serum be prophylactic and the disease against which protection is sought does not develop no confusion should arise The real difficulty lies in distinguishing neurological phenomena due to sera given therapeutically in certain diseases from similar phenomena which may result from the diseases themselves At times the distinction may be well nigh impossible as e g in meningitis treated with serum when organisms persist in the spinal fluid If the symptoms increase as the organisms disappear they may be attributed properly to the serum

Roger Mattei and Paillas[1] after studying nine cases which they attribute to antidiphtheric serum offer the following differential criteria in the presence of diphtheria Diphtheritic paralysis is not uncommon and occurs relatively late It is almost always ushered in by velopalatine paralysis and trouble with accommodation and often is widespread and worse in the lower extremities It is moreover constant until recovery occurs Serum paralysis is rare in diphtheria tends to come on earlier involvement of the palate and of the muscles of accommodation is rare and often it is confined to the brachial plexus on both sides They note the medicolegal importance of the distinction but admit that in borderline cases it may be impossible to make

With regard to a similar differentiation in tetanus Muller and Quenec[44] state that the study of the electrical reactions in the muscles involved is the key to the problem If electrical hypoexcitability be present the paralysis is due to the serum if hyperexcitability it is due to the tetanus At times a therapeutic test may be decisive as in a case reported by the writer[45] The patient had erysipelas complicated by acute suppurative otitis media She had been treated with antistreptococcic serum and developed symptoms strongly suggesting brain abscess soon followed by urticaria A dose of epinephrine was followed by the speedy disappearance of the symptoms suggestive of brain abscess

tremities especially the deltoid supraspinatus and infraspinatus muscle Not infrequently it resembles an Erb Duchenne paralysis of acute onset Atrophy of the muscles involved fibrillary contractions and complete reaction of degeneration occur in the well marked cases Pains often extremely violent may shoot through the arms They may be of a strangely intermittent character In one case observed by the writer the patient would be wild with pain at one time and a few hours later state that she was perfectly comfortable except for her dread of the return of the terrific pains The paralysis too may be intermittent In the case of the patient just mentioned one of her nurses thought she was malingering because at one moment she would say she could not use her arms and a short time afterwards would move them freely In the worst cases the paralysis is more constant and clears up more gradually Objective sensory changes may occur also chiefly small areas of anesthesia

Mononeuritic Type — In this form a single nerve is affected the circumflex being especially liable with the usual symptoms of circumflex neuritis Sciatica paralysis of the abductors of the larynx unilateral or bilateral paralysis of the palatal muscles and nerve deafness also have been reported

Polyneuritic Type — Here there is a widespread involvement of the nerves giving rise to extensive syndromes such as flaccid quadriplegia etc

The *central nervous symptoms* exhibit a great variety of clinical findings as might be expected Aphasias convulsive attacks cord paraplegias meningism choked disc psychotic phenomena etc have been noted Rolleston[40] states that in a series observed by him 15 5 per cent of patients with serum sickness following intrathecal injections of antimeningococcic serum showed a recrudescence of meningeal symptoms without the reappearance of organisms in the spinal fluid Moricheau Beauchant and Fagart[41] have described a fatal case with central nervous phenomena in which death occurred sixteen days after a prophylactic dose of antitetanic serum Pagniez and Lerond[4] cite the case of a man with carcinoma of the mediastinum in whom serum sickness produced Jacksonian fits pointing to metastatic growths in the brain which had been completely silent up to that time A few cases resembling ascending myelitis have been reported as following serum injections While some of these may have been infections Lerond[41] has recorded an especially interesting case of an ascending paralysis reaching the face which came on after the injection of antitetanic serum and which after reaching its maximum showed a rapid improvement in the extremities with much slower recovery in the face

anaphylactic shock appear. Levy[48] advises ephedrine by mouth at least an hour before injecting serum and repeats it at frequent intervals after injection.

Desensitization. — When the need of serum is urgent in sensitive patients Mackenzie[49] suggests the following desensitization technic using a tuberculin syringe for the small doses and giving the serum as follows every half hour: *subcutaneously* 0.025 c.c., 0.05 c.c., 0.1 c.c., 0.4 c.c., 0.8 c.c., 1 c.c.; then *intravenously* 0.1 c.c., 0.2 c.c., 0.4 c.c., 1 c.c., 2 c.c., 4 c.c., 8 c.c., 16 c.c., unless the desired dose is reached before this amount is given or a reaction occurs. Epinephrine should be at hand constantly while desensitizing.

A sensitive patient should be desensitized every time serum is given no matter how short the interval between doses. It has been stated frequently that it is perfectly safe to reinject serum into any patient within ten days or less after a prior injection that produced no untoward effect. Generally this is true, but exceptions occur. Brindle and Jackson[50] report two cases of serum anaphylaxis in which the second dose followed the first by only two and three days respectively. Both were given epinephrine and recovered. It is well to use the most highly refined and concentrated preparations available. It seems probable that the recently developed "superconcentrated" sera will tend to diminish untoward reactions of all types. Skin tests seem to be of little or no value in determining those cases which will develop neurological symptoms. Kennedy[70] suggests giving sodium carbonate intravenously before injecting any serum following a suggestion of some of the earlier French writers. *The author has never used this. To prevent local muscle spasm in children* he often gives a dose of paregoric after the serum, repeating it as needed during the ensuing night.

Treatment

In the severest cases of anaphylactic shock artificial respiration must be resorted to at once. The immediate subcutaneous injection of epinephrine hydrochloride also is imperative, from 0.5 to 1 c.c. of a 1:1000 solution being the dose. In extreme cases 0.3 c.c. may be given intravenously. For infants 0.3 c.c. subcutaneously is not too much. The epinephrine should be followed promptly by a full dose of atropine sulphate, gr. 1/50 or even 1/30 for an adult, subcutaneously. The epinephrine may be repeated frequently at hourly or even half hourly intervals for a few doses if required. If the patient be cold external heat should be applied.

Prognosis

Park[46] states that collapse occurs in 1 case in 20 000 injections and proves fatal in 1 out of 50 000 injections Ramon[47] estimates 1 death in 100 000 injections In anaphylactic shock every minute the patient lives beyond 15 or 20 minutes increases his chance for recovery It is rare for the symptoms of serum disease to persist longer than three or four weeks and often they clear up in a few hours to a few days With involvement of the nervous system however the duration of symptoms may be increased materially Recovery may be very slow but is almost sure in the peripheral nervous types and even in the central types in which practically all the few fatalities from nervous involvement have occurred the outlook is better than the gravity of the symptoms might suggest Permanent residual paralysis is exceedingly rare and when it occurs very slight Complete recovery may be expected in from one to eighteen months usually in from two to four months

Prophylaxis

It is questionable whether much can be done to prevent the delayed reactions Every effort should be made to avoid anaphylactic shock A searching inquiry should be made for a history of any kind of allergic condition in the patient not omitting the question of sensitivity to horses If an allergic history exists serum should be administered only when indications are urgent Skin tests should be made before giving serum except in unusual emergencies One drop of serum may be injected intradermally and fifteen minutes allowed to elapse A wheal with any pseudopods should be considered as evidence of sensitivity In known allergics especially if sensitive to horses it is well to dilute the test serum 1 10 with sterile physiological salt solution and inject only one drop of this solution as death has been reported following a test injection of 1 drop of undiluted serum Some manufacturers as e g Lederle Laboratories Inc include such a test solution in a package of highly refined super concentrated serum The writer prefers such a package The ophthalmic test of putting one drop of serum in one eye and watching fifteen minutes for conjunctivitis may be used if preferred The author has no experience with it In a sensitive person if a heterologous serum be available it should be used If not and the need is urgent an attempt at desensitization should be resorted to with the utmost caution A rule of the first importance in serum therapy is that *provision always should be at hand for the immediate injection of epinephrine* should the symptoms of

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If edema of the glottis develops provision should be made to meet the emergency of threatened suffocation Scarification of the glottis may give relief if this fails to do so or in case no one is available who can carry this out tracheotomy will be needed If this situation develops there will be very little time to act hence anticipation of and previous preparation to meet this emergency is needed It is wise to have the necessary instruments at hand sterilized and so ready for immediate use

In central nervous cases developing symptoms presumably due to cerebral edema the intravenous injection of 20 c c of a 25 per cent solution of magnesium sulphate has proved of value in the writer s hands Hypertonic glucose may be used also In the peripheral types measures to relieve pain usually are imperative Morphine is contraindicated for any length of time because of the risk of addiction Large doses of codeine however are much freer from this danger and may be used Ephedrine combined with one of the barbiturates such as amytal is worthy of trial

Calcium therapy with vitamin D added to facilitate the utilization of the calcium may be given Whether heat by producing congestion tends to increase the development of edematous areas or not may be an interesting theoretical question but practically it often gives great relief especially as radiant heat or diathermy The former may be accompanied by gentle stroking massage but heavy massage is contraindicated until convalescence is well established The author believes that usually it is wise to tell the patient early that recovery will be slow but may be expected confidently This enables the sufferer to become reconciled to his situation and relieves him of the mental conflicts that may arise if he feels that his case may not be understood properly and that he is not making satisfactory progress

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CHAPTER VII

BRONCHIAL ASTHMA

BY I. CHANDLER WALKER

TABLE OF CONTENTS

Our present conception of bronchial asthma differs in many ways from that which has been handed down unchanged for many years. Moreover a careful analysis of the symptomatology in each case lends so much to the diagnosis of the probable cause that it seems well worth while to describe the clinical aspects in considerable detail

lung is normal An examination of the blood may reveal an eosinophilia but this is of little diagnostic importance

Pathology so far has not advanced our knowledge of this condition but animal experimentation however has enlightened the subject tremendously Brodie and Dixon[1] have shown that the vagus is the only motor nerve to the bronchial muscles and that in this nerve run two sets of fibers the constrictor and the dilator Examination of the sympathetic gave negative results so far as the bronchial muscles were concerned They found that stimulation of the constrictor fibers of the vagus could be excited by various irritants of the nerve itself or of the respiratory mucous membrane and a typical attack of spasmodic asthma would result — prolonged expiration distended lungs dry rales absence of excessive secretion in the bronchi no engorgement of the lungs Auer and Lewis[2] produced a stenosis of the small bronchi which was caused by spasm of the muscle fibers encircling the tubes Sewall[3] has shown that guinea pigs especially after previous sensitization may react to intranasal instillation of horse serum by the development of typical attacks of bronchial asthma such as have been described above Therefore by putting these findings together protein applied in the upper respiratory tract of a sensitized animal (Sewall) irritates the constrictor fibers of the vagus (Brodie and Dixon) producing a stenosis of the small bronchi by causing a spasm of their circular muscles (Auer and Lewis) the mechanism of a typical attack of true bronchial asthma is explained

In the above explanation the only term used that has not been defined is the word sensitized and a few lines will suffice to understand this word Magendie[4] in 1839 and Richet[5] in 1902 found that the first dose of a protein given to an animal was followed by a condition of markedly greater susceptibility to that protein This phenomenon is called anaphylaxis the animal is sensitized by the first dose of protein and is shocked by a properly spaced second dose of that protein The anaphylactic shock is due to the meeting of a specific antigen (the second dose of protein) with its antibody (produced by the first dose) and the resulting reaction gives rise to a toxic product which causes the characteristic symptoms Anaphylaxis therefore consists simply in the cellular reaction due to the fixation of antigen by cellular antibody In true bronchial asthma we now know that the patient is previously sensitized to some protein but we do not know why and furthermore we do not know whether it is the whole protein itself or the toxic product which is produced when the protein meets its antibody or a toxic split product of the protein (Vaughn[6]) that irritates the nerves innervating the bronchi Further discussion on this point at present would be endless and futile but it is certain that the causative agent in the production of an attack of true bronchial asthma concerns a protein

Atypical Bronchial Asthma or Asthmatic Bronchitis

There is another type of attack commonly met with in patients who in the past have been considered as bronchial asthmatics but who have not ac

Types of Asthma

Typical Bronchial Asthma

An attack or paroxysm of typical or true bronchial asthma consists of the following cycle of events Some type of foreign protein, acting either centrally or peripherally as an irritant on the nerves that innervate the smooth muscle tissue lining the bronchi causes a spasm or constriction of the bronchial musculature The muscles of inspiration are equal to the task of drawing air through the constricted bronchi into the air cells of the lungs, but the elasticity of the lungs, together with the muscles of expiration are not sufficient to expel the inspired air in the normal time so that expiration becomes prolonged and is finally interrupted by an inspiration before the normal amount of air has left the lungs Consequently, as the attack progresses the lungs become overdistended with residual air and sooner or later this overfilling of the lungs with air causes labored inspiration, although expiration remains more prolonged and more difficult than inspiration The attack is now at its maximum and it may continue for only a few minutes or for a few hours At the height of the attack the patient may develop a dry cough which in a short time may become productive in raising a more or less characteristic type of sputum This sputum is thin clear slightly tenacious and in it are suspended small white masses of mucus resembling tapioca and called Laennec s pearls Usually there are quantities of eosinophiles present in the sputum, but they are of little diagnostic significance since they may be present in any sputum nasal secretion or inflammatory exudate Charcot Leyden crystals Curschman s spirals, and bronchial casts are not found frequently enough in such sputum to be of diagnostic importance The attack of asthma begins to subside when sputum is raised There is no fever and only a slight elevation of the pulse rate accompanying the attack After the attack has subsided, the patient may be more or less fatigued but is otherwise normal and free from all symptoms until another attack is suddenly precipitated hours days or months later depending upon when some foreign protein is again encountered

On physical examination during an attack of typical or true bronchial asthma inspection verifies what has been already described, and in addition there may be some cyanosis Percussion of the lungs during the height of the attack reveals a high pitched resonance On auscultation expiration is prolonged and feeble and inspiration is wheezing and accompanied by dry rales after expectoration has developed there may be moist rales Fluoroscopy of the chest at the height of the attack reveals a motionless diaphragm which seems to be fixed in a depressed position and the lungs expand very slightly on inspiration An analysis of the patient s alveolar air shows a low carbon-dioxid content although the blood at the same time shows a normal carbon dioxid content After the attack has subsided fluoroscopy of the chest and analysis of the alveolar air show normal findings and the vital capacity of the patient s

atypical asthma or asthmatic bronchitis is as follow The bacterial infection in the bronchi causes the usual type of bronchitic sputum which may be thick, but it is not very tenacious or jelly like and it is raised with little difficulty ordinarily when the patient is not sleeping At times however the sputum becomes very tenacious and jelly like and it clings so tenaciously to the lumen of the bronchi that repeated coughs may fail to remove it The stimulus to coughing however is so great that the patient repeatedly coughs and the more he coughs the more dyspneic he becomes until finally the tenacious secretion is raised after which the patient rapidly becomes free from dyspnea There is probably a slight constriction of the bronchial muscles since the inhalation of fumes from antispasmodic remedies is followed by the raising of sputum and consequent relief from dyspnea These drugs release the muscular constriction thus leaving the secretion unattached This muscular constriction however is not as marked as it is in the typical bronchial asthma as first described neither is it caused by protein irritation of the nerves supplying these bronchial muscles The cause of this slight muscular constriction in the atypical cases probably results from local irritation due to the protracted spell of coughing or less likely it is due directly to the irritation of the tenacious sputum

The dyspnea in these attacks is chiefly inspiratory in type and is due partly to the unproductive cough and partly to the narrowed lumen of the bronchi this narrowed lumen is due partly to slight muscular constriction and partly to the coating of tenacious mucus superimposed upon the constricted mucous membrane of the bronchi After the acute attack has subsided the patient is not entirely free from symptoms he still has more or less cough and expectoration until another attack occurs this may be a few hours later or not until the early morning hours of the next night The duration of the attack may be a few minutes but more commonly it lasts an hour or two and frequently the patient may continue in a more or less acute attack for several days These attacks are frequently accompanied by a little fever and a slightly elevated pulse rate

Physical examination of patients afflicted with this atypical type of bronchial asthma reveals during the interval between attacks signs of chronic bronchitis and emphysema During the attacks the dyspnea is chiefly inspiratory in type, although both inspiration and expiration are prolonged but the patient manifests the greater effort on inspiration and in addition to the wheezing and dry rhonchi there may be heard coarse bubbling rales in the bronchi The patient himself describes the dry râles as whistling and the wet râles as rattles Fluoroscopy of the chest during the attack reveals a diaphragm fixed in about the normal position midway in its greatest excursion thus indicating no great amount of distension of the lungs The lung vital capacity is low in these cases between the attacks at a time when the patient is most free from symptoms this indicates a state of permanent emphysema

Pathology so far has revealed with the exception of peribronchial thickening nothing in addition to what may be determined on physical examination By

cording to our present knowledge, true spasmodic attacks of bronchial asthma as previously described Careful observation and study brings out marked differences between this type of attack, which is about to be described, and the true bronchial asthmatic attack already described In the past these two distinct types of attacks have not been separated and consequently confusion has resulted Even at present one must not be too dogmatic and entirely divorce this type of so-called bronchial asthma from the true type already mentioned Nevertheless the term asthmatic bronchitis would best describe this type of case In other words the type of attack already described, must be called true or typical bronchial asthma and the type of attack, about to be described should be called atypical bronchial asthma or, possibly better still asthmatic bronchitis

This atypical attack of bronchial asthma is usually associated with respiratory infections such as colds and bronchitis chronic bronchitis catarrhal conditions of the nose and throat and occasionally with infections of the teeth tonsils and sinuses and rarely with infections located in any part of the body The primary cause is bacterial infection Proteins are not the cause of this type of asthma with the exception that occasionally bacterial protein may be the cause and therefore in only these occasional cases may this type of asthma be anaphylactic

Patients with this type of asthma usually develop their attacks in one of two usual ways The most common manner is as follows The patient has been subject to bronchitis for a period of months or even years During this time the symptoms of bronchitis have progressed and have become more and more severe At first possibly there may be only a slight unproductive cough which may have followed a neglected cold later the cough is more annoying and may become productive of expectoration There may or may not be slight fever and the patient since physical signs are practically negative may be suspected of having tuberculosis After a time there is some difficulty in breathing especially on exertion Later still respiration becomes wheezy and dry rhonchi are heard on auscultation If these symptoms progress no furthe the condition is called bronchitis If however the patient develops attacks of dyspnea (it is inspiratory in type) and suffocation with or without exertion the condition is called bronchial asthma In reality the condition is a severe type of bronchitis and does not closely simulate typical bronchial asthma the condition is more correctly asthmatic bronchitis

The manner, next most common to the above in which patients develop this kind of asthma is as follows As in the above case the patient becomes subject to chronic bronchitis and although he is more or less troubled with it during the time he is awake he is usually free from attacks of marked dyspnea and suffocation, but during his sleep the attacks appear and usually awake him in the early morning hours this type of asthma most usually develops during or past middle age

The sequence of events which takes place in these two types of attacks of

Protein Sensitivity

Determination of Protein Sensitivity

There are several methods of determining whether a patient is sensitive to a protein or not One way which is used more or less is the intradermal or intracutaneous injection of the protein there are however some objection to this method and it tends to be too delicate if not non specific A test which is used more extensively and which is very reliable is the cutaneous or skin test which is performed in the following manner A number of small cuts each about an eighth of an inch long are made on the flexor surfaces of the forearm These cuts are made with a sharp scalpel but are not deep enough to draw blood although they do penetrate the skin On each cut is placed a protein and to it is added a drop of tenth normal sodium hydroxid solution to dissolve the protein and to permit of its rapid absorption At the end of a half hour the proteins are washed off and the reactions are noted always comparing the inoculated cuts with normal controls on which no protein was placed A positive reaction consists of a raised white elevation or urticarial wheal surrounding the cut The smallest reaction that we call positive must measure 0 5 cm in diameter All larger reactions are noted by a series of plus marks and any smaller reaction is called doubtful

As evidence that the skin test is satisfactory and conservative we have found by treatment with subcutaneous injections of proteins that we cannot inject a patient with a stronger solution of a protein than that which gave a positive reaction without provoking an attack of asthma and that a series of treatments with weaker solutions which failed to give a positive skin test produces no benefit

The cutaneous or skin test therefore separates true or typical bronchial asthma from the atypical or asthmatic bronchitis The patient with the typical variety gives a positive skin test with proteins and is therefore sensitive to those proteins which are the direct cause of the asthma whereas the atypical variety fails to give a positive skin test with proteins thereby excluding proteins as a direct cause of asthma

Rarely one will test a patient who reacts positively to every protein tried but the normal control cut will also be positive so that such positive reactions must be discounted False positive reactions in such patients that react to all skin cuts are due to temporary irritability of the skin since at another visit later on the skin tests may be done satisfactorily Fortunately such cases are rarely encountered Frequently patients give a positive skin test with one or more proteins that have no bearing on the cause of the asthmatic condition, but these proteins are the cause of the eczema urticaria or hay fever conditions which complicate and are associated with asthma in those particular individuals

animal experimentation Oftedal[7] has demonstrated an elective affinity of bacteria (streptococci) for the bronchial musculature the streptococci were obtained from the sputum of patients who had the atypical type of bronchial asthma

If all cases of bronchial asthma could be placed as easily in either of the two groups as already described, namely typical and atypical the disease would now be comparatively simple from the standpoint of cause, prevention, and treatment Unfortunately this is not the case The description of the atypical variety holds for all cases of that type in that it is a chronic condition from the beginning the patient s symptoms are no different after he has had the disease for years than they were with the first attack The true or typical bronchial asthmatic when the condition develops during childhood or thereafter, presents the typical attack as already described until, because of frequently repeated exposure to the causative protein he has frequently repeated attacks Frequently repeated attacks sooner or later cause so much bronchial irritation that bacterial infection gets a hold and a resultant chronic bronchitis is superimposed upon a true bronchial asthma When this occurs the patient may present symptoms closely simulating the atypical variety The history, which may be elicited from the patient describing the onset and the first attacks of the condition will aid in determining the kind of asthma, and the cutaneous or skin test will definitely determine the kind of asthma

Asthma in infants and very young children frequently presents at first a condition of frequent colds or bronchitis even though the cause is anaphylactic in nature and not due to bacterial infection This is probably so because the infant s bronchial mucous membrane and respiratory mechanism is easily irritated (a protective mechanism which is not necessary after intelligence is more fully developed) and more probably so because asthma in infants and very young children is usually caused by foods which are so frequently eaten that the condition is chronic from the beginning

Furthermore since such a young individual spends most of its time sleeping by itself especially after eating it is possible that he could have true attacks of bronchial asthma from food proteins for some time long enough to produce a constant bronchitis before the immediate family might recognize any ailment An adult who has bronchial asthma from food proteins, rarely if ever vomit as a result of eating those proteins but infants and young children frequently vomit following the ingestion of some protein which, if persistently eaten or even not eaten for a long time later on causes typical bronchial asthma The act of vomiting in these cases is evidently another illustration of protective mechanism since Schloss and Worthen[8] have found that the gastroenteric tract of infants is permeable to undigested foods Further discussion of the clinical symptoms associated with the two types of bronchial asthma will be considered more specifically later on

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Occasionally a patient is met with who gives a positive skin test with a protein that apparently has no bearing at all on that patient's condition. A case in point is worth mentioning. A woman who was sensitive to the protein of cornmeal and staphylococcus pyogenes aureus never ate cornmeal, and treatment with vaccines of staphylococcus pyogenes aureus relieved the bronchial asthma for many months; then the attacks reappeared worse than ever. Treatment with the vaccine, however, brought no benefit. On account of the conservation of wheat flour during the war this patient had to eat substitutes and she was eating cornmeal breads freely without thinking about the positive skin test with that protein. On being reminded about that positive test she omitted cornmeal from her diet and the attacks of bronchial asthma stopped and have not returned.

Another rare type of patient is one who gives a positive skin test with a protein but is able to eat sparingly or moderately that particular protein without having symptoms, but when that particular protein is eaten in excessive amounts attacks of bronchial asthma result. Therefore positive skin tests by proteins which seem to have no bearing on the cause of asthma should be considered as danger signals and not as false reactions, such positive tests should not be disregarded. Absolute omission of a food from the diet for some time often changes a positive skin test to a negative or only slightly positive test. This is important to bear in mind since sometimes, the evidence is so strong that a food causes symptoms that that particular food is omitted from the diet before skin tests are made, then a negative skin test is obtained with that food and that is misleading. Therefore when testing with food proteins the patient should be eating them and slightly positive reactions should be repeated at another time.

Proteins Causing Sensitivity

In order to be absolutely sure that a patient is not sensitive to any protein, almost an unlimited assortment of proteins is required, as the following statements will disclose. The same patient is not equally sensitive to the individual proteins found in the same type of animal hair. Only twenty per cent of these patients that were sensitive to horse dandruff were also sensitive to the whole horse serum protein, so that a very small percentage of asthmatics is sensitive to horse serum and the danger of injecting an asthmatic with moderate amounts of horse serum, such as antitoxin, is confined to only a rare case. The sensitization of patients to different tissues or fluids of the same animal also varies. Taking for example the beef animals the same patient may be sensitive to any one alone or to any combination of the following tissues or fluids, namely meat, milk, serum and hair. The same holds true for the fowl in regard to feathers, meat and egg, and for the sheep in regard to wool, meat, and serum.

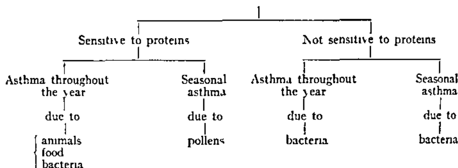
The same patient may be sensitive to any one alone or to any combination of the different structures of the plant namely to the seed pollen and the leaves Patients differ in their sensitization to the individual proteins of the same cereal for instance the same patient may be sensitive to any one alone or to any combination of the individual proteins of the wheat kernel The above examples show the specificity of the skin test separating more or less closely related protein but they do not really represent examples of multiple sensitization The term multiple sensitization should be restricted to sensitization with proteins that are less closely related For example the same patient may be sensitive to any combination of the proteins derived from plant animal food or bacterial sources thus we have a combination of widely separated proteins This type of multiple sensitization is very common and these cases are the most difficult to treat

Entry into the Body of Proteins Causing Asthma

The sources through which proteins that cause bronchial asthma enter the body are *inhalation ingestion absorption and infection* *Inhalation takes place* through the respiratory tract and chiefly concerns the protein in the pollen of plants in the emanations and hair of animals in the flour of cereal grains and in organic dust Ingestion has to do with the protein of food and we know that foods after entrance into the gastro-intestinal tract do cause asthma Absorption apart from inhalation and ingestion concerns the conjunctivae and to a less extent the skin By infection we mean the presence of pathologic bacteria in any part of the body but more especially foci of infection located in the teeth tonsils nose throat and lungs In the case of bacteria we have to deal with the protein element as well as with the infectious element The skin test has to do only with the protein element so that even though bacteria give a negative skin test they still may be a cause of asthma through their infectious nature and the patient need not be sensitized to bacterial protein Through inhalation the protein acts as an irritant on the peripheral endings of the constrictor nerve fibers through ingestion and absorption the incompletely digested proteins by circulating in the blood stream probably act upon the central end of the constrictor nerve fibers and through infection the bacterial protein may act either or both ways

Classification of Causes of Bronchial Asthma

By means of the cutaneous or skin test the causes of bronchial asthma may be classified in the following manner and the true or sensitive type may be separated from the atypical non sensitive type or asthmatic bronchitis



Of the first six hundred patients tested by the author forty eight per cent gave positive skin tests with some type of protein and the remaining fifty two per cent failed to be sensitive Other observers have since reported similar results Pediatricians however naturally find a larger per cent of positive tests since sensitization is much more frequent in infants and young children Furthermore those physicians who practice in very warm climates, where pollens are prevalent most of the year find a very high per cent of positive tests Kahn in Texas feels that every case that he sees is sensitive to some pollen One who comes in contact only with adults will obtain a very small per cent of positive skin tests since the majority of adults have the asthmatic bronchitis type of asthma

Animal Emanations Causative of Asthma

It is quite frequent to find that asthma is caused by exposure to the hair or dandruff of animals Horse hair protein seems to be the most frequent cause and cat hair and feather protein seem to be the next in frequency Dog hair and wool protein sensitization are sufficiently common to justify including these as a routine test Cattle hair, mouse hair bird feathers rabbit hair guinea pig hair goat hair and fur protein have all been reported as causative of asthma Although the patient may not know that he is exposed to any animal hair he may give a history of having pets at home or of using pillows that are filled with various types of hair or feathers

Food Proteins Causative of Asthma

Of the food proteins which most frequently give positive skin tests, egg wheat and milk are the most common With the egg it is most often the white that reacts, but the yolk reacts often enough to be used routinely in testing With milk, sometimes it is the casein but just as often if not oftener it is the lactalbumen therefore these two elements of milk should be tested separately Although wheat is the most usual cereal grain to give a positive test, the protein

of rice oats barley rye and corn react sufficiently often to warrant including these in a routine test Of the meats beef seems to be the most important and chicken next in order of frequency However, lamb mutton pork duck, goose and all kinds of game have been known to cause asthma but most of these need not be tested for without some lead as to their being a cause or unless they are frequently eaten The last statement hold true equally well for fish Fresh water fish rarely cause asthma salt water fish often cause asthma shell fish especially lobster very often cause some type of sensitivity

Although any of the vegetable food proteins may cause asthma it is those that are most frequently eaten that should be included in a routine test Potato bean and pea most frequently give positive skin tests In order to avoid testing with every vegetable it is advisable to inquire from each respective patient as to those vegetables most frequently eaten and those suspected of causing symptoms As an example the author had a patient who was very fond of raw carrots and ate them daily carrot protein gave a positive skin test and omission of carrot was followed by complete relief of asthma

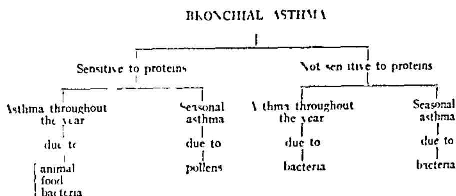
Although any of the fruits may cause asthma none are met with sufficiently often to justify special attention The patient s history will help to determine whether some seasonal fruit might be a cause and the fruits that are eaten during most of the year may be used in the routine test As an example of extreme sensitiveness to fruits the author has had a patient who was so sensitive to lemon that a few drops used to disguise the taste of half a glass of magnesium sulphate caused symptoms lemon protein gave a positive skin test but citric acid did not

Among the accessory foods cocoa and chocolate quite often give positive reactions whereas tea and coffee very rarely react Of the nuts peanut is the most usual to cause asthma although almond pecan and walnut occasionally react The author has several patients who have asthma from eating honey and other similar cases have been reported The author has had a patient who was very sensitive to mustard and had asthma only when she ate mustard Not infrequently mayonnaise causes asthma Cheese frequently causes asthma as also does goat s milk

Bacterial Proteins Causative of Asthma

Although not infrequently bacterial proteins do give a positive skin test, this does not occur as often as it seemingly should It is quite probable that the manipulation of the bacteria necessary to obtain a pure dry protein destroys the anaphylactic property Cutaneous tests with bacterial proteins do not seem to be worth doing Intracutaneous tests with killed bacteria do however seem to be worth doing

Thomas Famulener and Tonart[9] have obtained excellent results using killed bacteria intradermally These authors isolate the various organisms by culturing the sputum on human blood agar slants and vaccines are prepared of each



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must be noted by touch as well as by sight and recorded graphically as they change from day to day

Any of the following features may appear about the point of injection during the first twenty four hours and may persist for five or more days following the test (1) an indurated slightly elevated nodule about 0 5 cm in diameter (2) redness of the skin over the nodule (3) a surrounding pink flush or zone of erythema from 1 to 10 cm in diameter the so-called areola (4) tenderness on pressure usually occurring at the nodule only but sometime extending over the whole areola (5) heat felt by the palpating finger (6) lymphangitis lasting from one to three days not necessarily associated with a pustule but commonly with enlarged tender gland (7) slight fever and malaise occasionally accompany marked late positive reactions (8) pustule

Late reactions to the different types of organisms vary somewhat Staphylococci and streptococci regularly but the intestinal group of bacilli less often produce the indurated pustule Positive reactions to bacilli of the colon typhoid group give large hot areolae which fade in two or three days or more The nodules caused by streptococci frequently persist for many days or even weeks sometimes becoming pigmented and occasionally showing desquamation

Positive reactions whether early or late are considered to be of equal importance as indications for the therapeutic use of the vaccines which produced them

Brown has also found intradermal tests using killed culture of bacteria very satisfactory whereas Rackemann found this method unsatisfactory This difference of opinion is very likely due to differences in technique and to the fact that Rackemann used too large quantities of bacteria

Pollens Causative of Asthma

Since the same pollens that cause hay fever may also cause asthma rather than to repeat unnecessarily reference should be made to the following chapter chapter XIII Hay Fever where a detailed discussion of the pollens their seasons and respective localities is given It might be stated here however that frequently hay fever patients have a very slight attack of asthma at one time during their hay fever often hay fever symptoms end with a day or two of asthma and still others are more or less choked up at times during their hay fever Asthma caused by pollens may continue after the termination of the pollen season The continuation of asthma in these cases is due to secondary bacterial infection causing bronchitis in a patient whose resistence either local or general has been lowered because of prolonged severe pollen asthma

Miscellaneous Proteins Causative of Asthma

Orris root protein so frequently causes asthma that it should be included in routine tests Orris root is a constituent of most face powders An example of an unusual cause of asthma are the two following instances Two patients

organism both for testing and for therapeutic purposes "The standardization of the vaccine is based on the method published by Hopkins which offers a means by which an accurate measurement by volume of the thoroughly packed moist organisms may be made in a special type of centrifuge tube A one per cent suspension in physiologic sodium chloride solution is prepared from the measured packed bacterial residue then the organisms are killed by heat Controls for sterility are made after which sufficient tricresol solution is added to give an 0 25 per cent concentration Instead of standardizing the original one per cent suspension by determining the number of organisms present in 1 c c a unit valuation has been placed on the volume content of bacterial substance present in such a suspension The unit consists of that amount of bacterial substance which is present in 0 01 c c of a one per cent suspension of the organism prepared under certain fixed conditions Experience has shown that this quantity (one unit) of vaccine is perhaps the most favorable amount to produce a skin reaction when applied intradermally in the hypersensitive patient The one per cent suspension of killed organisms prepared by the Hopkins method is designated vaccine stock' and is supplied in small ampules for the intradermal tests The vaccines for therapeutic purposes are prepared from the vaccine stock which contains 100 units per cubic centimeter Dilutions in physiologic sodium chloride solution containing 0 25 per cent tricresol are made to include the number of units per cubic centimeter desired by the clinician

Emphasis must be placed on the exacting technical character of the laboratory work which demands the best efforts of a highly trained bacteriologist The clinician s success in diagnosis and treatment of the class of patients under consideration here is dependent on the full cooperation of the laboratory specialist

Each test injection is made with a freshly sterilized tuberculin syringe and a needle of fine calibre with which the control solution and each vaccine are introduced intradermally so that minute wheals are seen The amount of test vaccine used in each instance is regularly 0 01 c c As a control in each series of tests the same diluent of sodium chloride and tricresol solution is used as that employed in diluting the vaccines

The positive reactions following these tests are of two separate types (1) an early reaction appearing in from ten to thirty minutes and soon thereafter fading (2) a late positive reaction noticeable in twelve hours or less and at its height on the second day It persists for from two to five days and under certain circumstances for several weeks

1 The early positive reaction is a wheal at least 1 cm in diameter, with pseudopodia or grossly irregular outline sharply marked off from a surrounding pink areola Early positive reactions have been observed in thirty five of 134 asthmatic and hay fever patients (about 25 per cent), but are rarely seen in other than this type of patient

2 The late positive reaction is not unlike the Schick reaction in appearance but in order to read and interpret its significance the component features

Age of Onset of Asthma

The age of onset of bronchial asthma is very important and bears a definite relationship to sensitization Stated briefly four fifths of the patients who began asthma during infancy were sensitive to proteins two-thirds who began during childhood were sensitive one half of these beginning asthma during young adult life were sensitive one fourth of those beginning asthma during adult life were sensitive and none were sensitive that began asthma after the age of fifty As the age of onset of asthma increases the frequency of sensitization diminishes and conversely the number of non sensitive cases increases These facts have been borne out repeatedly by other investigators Sensitization to food proteins is by far most frequent during infancy and of the foods egg protein milk and cereal grains are the most important Talbot[10] in a series of forty five children who had bronchial asthma found the skin test positive with egg in twenty seven beef in five wheat in six horsehair in seven Koessler[11] and Rich[12] and many others report cases of asthma in young children caused by egg The frequency of sensitization to bacterial proteins was about the same for all ages of onset and the same was true of pollens up to adult age after which pollen sensitization was rare

Occupation in Relation to Asthma

Occupation may have a direct bearing on the cause of bronchial asthma and occupation frequently explains the development of sensitization after the age of forty which fact is otherwise not usual Bakers frequently become sensitive to and have asthma from the dust of the cereal grains with which they make pastry wheat protein is the one most frequently met with Hostlers sometimes become sensitive to horse hair protein Farmers sometimes become sensitive to pollen proteins and to the various grains that are fed to live stock The following examples which are rather unusual may be of sufficient interest to narrate as instances where occupation determined the cause of asthma A physician had asthma whenever he mixed a dose of salvarsan and gave a positive skin test with salvarsan A man whose work consisted of sifting green coffee beans became sensitized to the protein in the green husks and as a result had asthma Another man whose work was that of a jewel polisher became sensitized to the protein in the dust from the boxwood with which he polished the jewel and a second man working in the same room became sensitized to the protein in the dust from orangewood with which he polished jewels The man sensitized to boxwood protein was not sensitive to orangewood and vice versa The author has recently treated an entomologist who has asthma whenever he is exposed to gypsy moths and since this is his occupation he is more or less constantly exposed to them in the laboratory where they are hatched and studied This patient is very sensitive to the larval and pupal hairs and less sensitive to

whom the author has studied had asthma from the ink with which newspapers were printed In these cases the ink was very heavy and liberally applied Whenever these patients handled this particular newspaper they would have asthma but other newspapers did not affect them Campbell[42] has gotten positive skin tests with silk silk floss and Kapox very frequently in eczema patients Cooke[43] has definitely proved that dust frequently causes asthma and gives a positive intradermal test He collects the dust in a vacuum cleaner removes the fat with ether and then extracts it in the standard extracting fluid of Coca Coca's extracting fluid is sodium chloride 0 5 per cent sodium bicarbonate in a concentration that 10 c c of fluid equals 3 c c of tenth normal alkali and carbolic acid in a concentration of 0 4 per cent In a succeeding paragraph other proteins will be noted in their relation to occupation as a cause of asthma

Seasonal Non sensitive Asthmatics

In contrast with the seasonal sensitive bronchial asthmatics there are also seasonal non sensitive asthmatics who simulate the asthmatic bronchitis type and in many of whom bacteria have been proved to be the cause of the symptoms Usually this seasonal non sensitive type of patient does not exactly coincide seasonally with the sensitive seasonal type so that the time when the patient has asthma usually determines the cause In a few instances however the two types of seasonal asthma correspond so closely that it is essential to do skin tests with the pollens in all cases whose attacks of asthma are limited during the months from April to October Furthermore, bronchial asthma caused by pollens often continues after the termination of the pollen season The continuation of asthma in these cases is due to secondary bacterial infection as explained in the last paragraph There are three other seasons during which patients have bronchial asthma of the atypical type and during which no plants pollinate One season is during March and April and another is during October and November The very changeable weather at these two seasons causes colds and bronchitis which if severe enough, become asthmatic bronchitis The remaining season referred to extends from the first real cold weather in the fall until the first seasonable weather in the spring this is essentially a winter seasonal or type of asthma associated with bronchitis These seasonal varieties of asthma concern New England naturally in colder climates these seasons are advanced and in warmer climates they are retarded and at the warm winter resorts these seasons are reversed this applies to the pollen variety as well as to the non sensitive variety of asthma

Concerning the non sensitive asthmatic who has attacks throughout the year, nothing can be added to what has already been written earlier in this paper they do not differ from the non sensitive seasonal asthmatics except that they have continuous asthma and are usually past middle life when their attacks begin The condition is essentially a severe type of bronchitis due to bacterial infection in a patient with lowered resistance

have been mentioned There are however secondary or contributory causes of minor importance they are secondary and of minor importance because after treatment with the proper protein with which the patients are sensitive or if not sensitive after proper vaccine treatment patients become tolerant to such conditions and may be exposed to them without having asthma Patients with bronchial asthma associate attacks with cold air dampness changeable weather winds going from a hot room to cold room and vice versa menstruation indigestion biliousness distension of gastrointestinal tract overfilling of stomach nervousness irritability being overtired excitement dust irritating odors and gases colds and bronchitis and in fact anything that is not in perfect accord with the particular individual subject to asthma The explanation of these minor causes is that the patient who has had frequently repeated attacks of bronchial asthma or asthmatic bronchitis has as a result of these attacks a very sensitive delicate or easily upset respiratory tract and mechanism and the least deviation from the narrow limits of each particular case is apt to precipitate an asthmatic attack The vital capacity of the asthmatic is greatly reduced As one theory puts it there is an unbalance of the autonomic nervous system but whatever the condition may be it is restored by proper treatment which removes the primary causes that have been discussed at length throughout this paper Although neurasthenic neurotic and psychoneurotic conditions are frequently associated with bronchial asthma these conditions are usually the result of bronchial asthma and although rarely they may be the cause they are not sufficiently often the cause to warrant a place among the causes of bronchial asthma

There seem to be two kinds of colds and of bronchitis one of which is anaphylactic and the other due to bacteria Relief or freedom from the first type follows proper treatment with proteins Frequently vaccines relieve and prevent the other type Adenoids infected tonsils teeth and sinuses catarrhal conditions and infections in any part of the body may be primary causes of bronchial asthma or they may be secondary causes by lowering the individual's resistance to bacterial infection in the bronchi This must be borne in mind and such condition should be remedied on general principles and for the general health of the individual Shivdas[14] has found pyorrhea alveolaris to be a cause of bronchitis and asthma and proper treatment of the condition resulted in marked improvement or disappearance of the condition

Theories of the Cause of Asthma

During the past few years Manwaring[15-20] has done a great deal of experimental research on the problem of anaphylaxis with the result that the following two phases may have a bearing on asthma in the human In addition to the well recognized anaphylactic syndrome caused by smooth muscle contraction there is evidence that an equally striking anaphylactic syndrome may be produced by suddenly increased capillary[1] and parenchymatous[18]

the fuzz of the egg mass as determined by the skin test A recent patient who manufactures the ingredients of home brew became sensitized to the dust of the malt but not to the dust of the hops Inoculation with a dilution of the malt protein relieved his asthma Those who are exposed to fur dyes sometimes have asthma through the inhalation of the dry powdered dye rather than from the fur itself as would be expected Peshkin[41] has reported the instance of a pharmacist who became sensitive to and had asthma from ipecac The author has frequently been told by asthmatic patients that aspirin would cause an attack but more often it seems to benefit or relieve asthma It is thus evident that probably any kind of protein may become a cause of asthma

General Considerations

The following general considerations are worthy of note The cases having the two types of bronchial asthma are equally divided between the two sexes and a little more than half of the males were sensitive and a little less than half of the females were sensitive it has already been stated that forty eight per cent of the total cases were sensitive The frequency of asthma is about the same for all ages it is just as frequent in children under the age of two as at any other age with the exception of the ages thirty five to forty five during which the largest number of cases developed the condition The nationality of the patient played no part in the cause or the frequency of the disease so-called neurotic races as for instance the Jewish race were no more liable to asthma than other nationalities The length of time that a patient has had asthma is important since one must bear in mind that the longer one has had asthma the more pronounced may be the resultant bronchitis and emphysema, so that the asthma may not be relieved by removing the offending cause but the bronchitis must also be treated Multiple sensitization is by far most frequent among those patients who began to have asthma during infancy, that is, it is quite frequent among those beginning asthma between the ages of two and five and five and ten but after these ages multiple sensitization is not very usual Sensitization to one protein early in life is apt to be followed by sensitization to other proteins early in life and vice versa non sensitization early in life is not so apt to be followed by sensitization later on

Eczema is a very common complication of bronchial asthma in young children and the presence of eczema with asthma is very strong evidence that some food protein is causing both conditions at this early age Blackfan[13] states that a history of eczema in early life is nearly always the rule with patients who are unable to take different foods on account of urticaria edema and asthma So many others have pointed out these facts that it is a well known observation

Contributory Causes

So far in this chapter only the primary or direct causes of bronchial asthma

from pollens Some of these patients were treated until the whole pollen gave no reaction at all and others until the reaction was only a slight one in no case however since treatment was omitted three or four years ago has the patient become more sensitive or had any asthma

In the non sensitive cases the only index we have as to results from treatment is symptomatic improvement The writer has many asthmatics who were treated with autogenous vaccines and with vaccines that contained the organisms usually found in the sputum of such cases that have been free from asthma for period of three four, and five years *following vaccine treatment*

With the non sensitive bronchitis type however the older the patient when asthma begins and the older he is when treatment is begun the more unfavorable the prognosis *from vaccine treatment The severity of the bronchitis* the degree of emphysema and the resistance of the individual to bacteria all modify the prognosis in the non sensitive type The sensitive type probably never dies in an attack and the non sensitive type rarely dies in an attack Neither does either type of case outgrow or spontaneously become cured of asthma when such results seem to occur they are actually due to the removal of the offending protein to a change in the patient s environment or to an increased resistance on the part of the patient toward certain bacteria which were causing the symptoms Acute infections *have no effect in the sensitive type* but in the *non* sensitive bronchitis type they may temporarily relieve attacks or they may precipitate attacks The incidence of pneumonia and tuberculosis is no greater in the asthmatic than in any other chronic disease neither does asthma predispose to these diseases Although the elasticity of the lung in an asthmatic after a time becomes impaired and thus makes the prognosis more unfavorable the integrity of the myocardium is rarely weakened

Asthma seems to be fatal in a very small percentage of cases In 1922 Huber and Koessler[44] reported the pathological findings in six cases of asthma in the literature they found fifteen fatal cases of asthma reported with more or less detailed microscopic study of these they considered only about half to be cases of true bronchial asthma In only four of twenty-one instances could death be attributed *with any degree of certainty* to uncomplicated bronchial spasm In 1923 Lemierre Leon Kindberg and Levesque[45] reported a fatal case of asthma *in a man who had intense dyspnea for ten weeks* In 1926 Rackemann[46] *reported five cases whose* deaths were apparently due to a severe attack of asthma these five instances were from a series of over one thousand cases seen over a period of six years The author does not know of a single instance of death during a severe attack of asthma of the few deaths that have occurred in asthmatics during the author s ten years experience heart trouble has been present occasionally but in most of the cases there was chronic bronchitis and emphysema and death seemed to be due more directly to the bronchitis and emphysema which may have caused heart failure than to asthma

permeability This is apparently the dominant factor in the production of the anaphylactic syndrome in dogs and in rabbits[17] Whether or not a similar mechanism could produce asthmatic or pseudo asthmatic symptoms in human beings we have no means of knowing, but if so, it would indicate the neces sity of a quite different method of therapeutic attack from that usually adopted

On perfusion of the blood free lungs of hypersensitive dogs with specific foreign protein the lungs invariably react with an explosive edema, usually accompanied by an active or passive bronchoconstriction[18] Nevertheless, no recognizable pulmonary reaction usually takes place on an intravenous injection of specific foreign protein into dehepatized hypersensitive dogs[19] Also a suffi cient amount of normal blood added to the perfusion fluid will invariably inhibit the anaphylactic reaction in the isolated hypersensitive lung [20] This indicate that there is an efficient anti anaphylactic mechanism in the extra hepatic tissues or body fluid presumably located largely in the blood stream If this finding applies to clinical asthma it might indicate that the determining factor in the precipitation of an asthmatic attack must be sought not in the hypersensitive condition of the pulmonary tissues but in a lowering of the normal defenses This again would indicate a new method of therapy and prophylaxis[7]

Koessler and Hanke [1] have been doing a good deal of research work with histamine They find that the normal colon contains a lethal dose of histamine and explains the freedom from illness of the normal individual by assuming that the normal mucus membrane of the colon does not permit of its absorption Where there is some pathology of the intestinal tract there may be absorption of histamine Wells [21] has pointed out that histidine is present in every normal protein and Ackermann [22] has found that histamine is a putrefactive product derived from histidine Barger and Dale [23] isolated from ergot what they identi fied as histamine and this when injected into animals stimulated constraction of non striated muscles such as those of the bronchioles Therefore histamine can produce anaphylaxis like symptoms and it is derived from histidine which is always present in the intestinal tract since it is present in every normal protein It is quite possible that this takes place in some humans and causes asthma

Prognosis in Asthma

Of those patients who are moderately sensitive to food proteins and care fully omit them for a time and then begin to eat them very gradually the majority seem to become desensitized and they remain free from asthma The author has observed over a period of years a number of horse asthmatics, who were treated with the horsehair protein until the protein failed to give any re action Some of these patients have so far been free from asthma for six or seven years are able to ride drive or groom horses without symptoms and they are still negative to horse hair protein tests A number of patients have also similarly been observed who formerly were sensitive to and had asthma

from pollens Some of these patients were treated until the whole pollen gave no reaction at all and others until the reaction was only a slight one in no case however since treatment was omitted three or four years ago has the patient become more sensitive or had any asthma

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Differential Diagnosis

Although an attempt has been made to define clearly in this article what is meant by bronchial asthma and asthmatic bronchitis a differential diagnosis may be necessary In laryngeal and tracheal obstruction the dyspnea is inspiratory and the stridor of the inspiration instead of the wheezing of asthma serve to differentiate these conditions The diagnosis of acute bronchitis from asthma in very young children is very difficult, as already mentioned, the skin test is of the greatest importance because if positive, and it is positive to some protein in four fifths of the cases who later on develop asthma, the bronchitis should be considered as an early symptom of bronchial asthma Emphysema past middle age produces symptoms similar to asthmatic bronchitis but the age of the patient and the degree of emphysema will differentiate Asthma and emphysema frequently coexist Enlarged bronchial glands in children may give rise to dyspnea but the thoracic dullness sometimes but by no means always present irregular fever night sweats and the roentgen ray aid in making the proper diagnosis Mediastinal tumors and aneurysms of the arch of the aorta by compressing the trachea or main bronchus may give rise to paroxysmal dyspnea cough and secondary bronchial infection all of which together simulate asthmatic bronchitis The brassy cough tracheal tug substernal dullness and heaving impulse as a rule serve to diagnose aneurysm though at times the roentgen ray and fluoroscopy are needed The substernal dullness roentgen ray and fluoroscopy will differentiate mediastinal tumors the roentgen ray and fluoroscopy are necessary to diagnose smaller tumors of the mediastinum and those of the lung and bronchi that at times produce dyspnea simulating asthma A foreign body in the bronchus may be suspected from the patient's history Physical examination often aids in the diagnosis the X ray gives a positive diagnosis for foreign bodies opaque to its ray and at times reveals evidence of a non-opaque foreign body The increasing application of bronchoscopy is of importance in diagnosing foreign bodies and tumors involving the bronchus In hysterical dyspnea both inspiration and expiration are short and there is no real dyspnea these patients show the usual criteria of hysteria

In chronic fibrinous bronchitis which is a rare condition the symptoms closely simulate asthmatic bronchitis with the exception that there is a marked cyanosis during the dyspneic attack and the sputum at times consists of nothing but bronchial casts An enlarged thymus in children may cause dyspnea Localized foci of tuberculosis in the bronchial gland may break down and cause peribronchial thickening or even an inflammatory process in the bronchioles upon which is developed a secondary infection which may give rise to symptoms simulating asthmatic bronchitis Pierson [4] has observed such instances but they are not frequent As a rule it ought not to be difficult to differentiate tuberculosis from asthma

Paroxysmal cardiac dyspnea consists of quick panting respiration and an

important factor in its cause is diminished vital capacity of the lungs (Peabody [7]) renal dyspnea is probably due chiefly to an acidosis (Peabody [8]) in hypertension paroxysmal dyspnea occurs none of these conditions should be called asthma the patient's history and a physical examination should determine the diagnosis in all Asthma may complicate both cardiac and renal disease but the asthmatic condition is entirely separate from the other two in other words, true cardiac and renal asthma probably do not exist.

Treatment of Asthma

The treatment of bronchial asthma consists of the following kinds preventive drug specific protein vaccine non specific protein operative procedures climatic and supportive of these the specific protein and the vaccine treatment are of prime importance Naturally sensitization cannot be prevented in the human However when an infant or child has symptoms of recurrent colds and bronchitis which fail to yield to ordinary medication that person should be tested for sensitization Neither should colds nor bronchitis be neglected in adults In the future there need be no excuse for not giving a person who develops asthma due consideration early in the disease rather than as has been the custom in the past allowing such individual to drift along in a neglected way

Drug Treatment

The drug treatment of bronchial asthma is most disappointing In the asthmatic bronchitis type potassium iodide in 0 6 gramme (10 grain) doses three times day is of considerable service This drug thins the secretion in the bronchi thus enabling the discharge of an otherwise thick tenacious sputum which when not easily raised causes choking up severe coughing spells and asthmatic attacks In other word potassium iodide favors free drainage from the bronchi with slight effort This drug however does not benefit the sensitive type of asthma which is not complicated by severe bronchitis The incorporation of small amounts of codein with the potassium iodide is serviceable in allaying undue irritation The most reliable and yet the most harmless drug that temporarily relieves the acute attacks of either type of asthma is epinephrin This is obtained as adrenalin chloride 1-1000 (Parke Davis & Co) and should be administered in one half to one cubic centimeter doses for adults repeated as often as necessary This drug should not be given intravenously nor intramuscularly and large doses should be avoided in children with whom 0 to 0 3 c c suffices as a rule Next to adrenalin chloride atropine subcutaneously in large doses is preferable Ephedrin has recently come into prominence as a substitute for adrenalin chloride and its great advantage is that it may be taken by mouth Miller [24] was the first in this country to publish in detail observations as to its clinical use More recently Thomas [25] has pub-

lished a clinical report which gives very satisfactory results in the use of ephedrin in controlling the acute attacks of asthma. If the patient himself can not use hypodermic medication he tends to rely upon patent medicines and so called asthma cures. The most serviceable among these seem to be the ones that contain stramonium leaves and saltpeter in the form of a powder, the fumes of which when burned are inhaled for the relief of the paroxysm. These fumes seem to be anti spasmodic in action and following their inhalation thick sputum is raised and temporary relief results. Calcium has been used empirically for a long time in the treatment of asthma with rather discouraging results. Pottenger[37] has done much work which favors the administration of calcium in asthmatics. More recently Brown and Hunter[38] have emphasized the fact that a considerable proportion of asthmatics have a calcium deficiency. These authors recommend calcium lactate, parathyroid and thyroid medication as a valuable addition to what has already been outlined in the treatment of asthma. Many other drugs might be mentioned, but they are less reliable.

Specific Protein Treatment

Specific protein treatment which is the most successful procedure consists of treating or desensitizing the patient with those proteins to which the individual is found to be sensitive by the skin or cutaneous test. Subcutaneous injections with the offending food proteins do desensitize but the process is a long and tedious one and this method is less satisfactory than the method of feeding proteins. Schofield[7] probably was the first to overcome sensitization with food proteins by feeding them. He gave his patients pills containing minute amounts of the offending protein gradually increasing the dose until large amounts were taken without symptoms. Although it required two years before the patient was able to eat a whole egg the cure seems to have been permanent. Rich[8] in the same manner accomplished similar favorable results in a year's time. The difference in the length of time depends upon the size of the initial amount which the patient can take without symptoms. Schloss[9] and Talbot[10] have had success with this kind of treatment, and Crover[11] has had some success by feeding the food protein in a liquid form. All of these writers were dealing with young children whose parents were sufficiently conscientious to make a go of it. The author has tried this treatment with adults but none have been conscientious enough to take the proteins per schedule for any length of time.

Absolute omission of the offending protein is entirely satisfactory and not nearly as difficult as might be anticipated. This problem is sufficiently important to warrant considerable detail. Patients who are sensitive to potato usually are able to eat baked potato even though boiled potato causes symptoms. Although raw milk may cause symptoms boiled milk will not and cream and butter both of which consist practically of only the fat in milk may be taken

Shredded wheat biscuit and thin slices of bread well toasted on both sides may be eaten, even though the patient is sensitive to wheat. The explanation of these variances is that very high temperatures destroy the anaphylactic properties of proteins. Probably the only common food protein which cannot be treated is that of egg because heat sufficient to destroy its anaphylactic property would make it non palatable and indigestible. Furthermore not all of the individual proteins that constitute a food cause symptoms in the same person, and some individual proteins which do cause symptoms may not be present in a certain food in sufficient amounts to cause symptoms. Such examples follow. In rice the only protein present in appreciable amounts is oryzenin (six and five tenths per cent); in oats glutelin represents eight per cent of the protein, whereas avenalin and prolamine each represent one and five tenths per cent or less of the protein; in corn zein is the chief protein (five per cent); in whole wheat gliadin and glutenin each make up four per cent, whereas in the embryo wheat proteose, globulin and leucosin are present respectively in three, five and ten per cent. The importance of doing skin tests with these individual proteins in the cereals is evident, and in the case of rice, if the patient were not sensitive to oryzenin he could probably eat rice without trouble, since the other proteins probably are present in rice in too small amounts to cause trouble. Usually the same patient is not sensitive to all of the cereals, so that if wheat must be omitted other cereals may be substituted. Often patients are able to eat small amounts of the offending protein, whereas large amounts cause symptoms; this fact has been proven to be true by Schloss and Worthen and by Talbot, to both of whom reference has already been made. Schloss and Worthen found the gastrointestinal tract of infants to be permeable to undigested protein when taken in large amounts, and Talbot found a threshold below which the eating of protein caused no symptom, but as the threshold was approached symptoms began to appear. These facts evidently apply to some adults, since the author by doing bismuth gastrointestinal studies on patients who were sensitive to wheat proteins found abnormalities in the tract such as ptosis, fixations, kinkings and the like, which favor stasis and premature absorption at such points. Another added factor is the finding by Maurel[22] that whole wheat bread is not digested and assimilated as well as that made from the intermediate grade of wheat flour bolted to seventy five or eighty five per cent; the author's experience in asthma coincides with this view. Therefore for all of these reasons, and more especially because of the permeability and abnormalities of the intestinal tract, omission of or at least the careful feeding of the offending protein is by *far the most reasonable treatment* of food asthmatics.

Bronchial asthma caused by animal emanations is treated very successfully by subcutaenous inoculations of the offending protein. Before this treatment can be given, however, skin or cutaneous tests must be done with varying dilutions of the particular protein in order to find out the initial therapeutic dose. These dilutions may be made with one hundredth normal sodium hy

droxide and a useful series of dilutions consists of 1-100 1-1 000 1-10 000 1-100 000 and 1-1 000 000 (one part protein diluted one hundred times, and so on with N/100 sodium hydroxide) Patients who give a positive skin test with the hair protein in a dilution no stronger than 1-100 are not usually treated because although intimate contact with that particular animal hair will cause asthma the patient can readily avoid such contact Those who are sensitive to animal hair proteins in a dilution of 1-10 000 and 1-100 000 and these are the usual dilutions to which patients are sensitive surely should be treated. The first treatment consists of 0 1 c c of the strongest solution that fails to give a positive skin test and each week the dose is gradually and slowly increased until about one cubic centimeter is given then the next stronger solution is given first 0 1 c c and gradually and slowly increasing up to the maximum amount before the next stronger is given and so on As the amount of treatment progressively increases the positiveness of the skin test progressively diminishes until if treatment is carried on long enough, the skin test becomes negative with concentrated protein and the patient becomes absolutely desensitized Improvement usually is noted after three or four doses sometimes not until after eight or ten doses and in an occasional case, where there is an extensive bronchitis vaccines are required in addition to the particular protein The above treatment is given to horse cat and dog cases, but with those who are sensitive to feathers wool and the hair or fur of other animals it is easier to avoid these than to treat with their protein

Pollen asthmatics are tested and treated in a similar way with the exception that such high dilutions are not required and treatment should in these cases be given preceding the pollen season rather than during the pollen season For detailed methods of pollen treatment the following chapter on Hay Fever (Chapter VIII) may be consulted

Patients who are sensitive to bacterial proteins are treated with vaccines of that particular organism the first dose being small and thereafter gradually increasing the dose Thomas [39] reports complete relief or material improvement in 87 per cent and failure in 13 per cent of asthmatic patients treated with autogenous vaccines that were indicated by the intracutaneous tests which have already been outlined Brown [40] reports complete relief in 51 per cent, improvement in another 39 per cent and failure in 10 per cent of asthmatics treated with autogenous vaccines that were indicated by the intradermal test As much care is required to increase gradually the dose of vaccine as is required in the animal cases and in either case if a particular dose causes much reaction that same dose should be repeated before giving an increased amount

The treatment of multiple sensitization or of those who give positive skin tests with several types of protein is a matter of judgment Patients who are sensitive to several types of animal hair should be treated with that type which gives the strongest reaction or with that type to which they are most intimately exposed With patients who are very sensitive to animal hair and also sensitive to food protein the latter should surely be omitted and treatment with the

former is usually indicated as well. Those sensitive to pollens should always be treated even though food and animal proteins are also the cause. When bacterial proteins complicate the situation vaccines of such bacteria may be required.

Reference has already been made to the occasional necessity of treating sensitive cases who have marked bronchitis with autogenous vaccines made from the sputum. With the non sensitive or asthmatic bronchitis type of case autogenous vaccines are the best mode of treatment and good results follow their administration in at least two thirds of the cases provided the proper organism is given. In making autogenous vaccines thick masses of sputum which are raised at the end of an attack or come from the smaller bronchi are washed in sterile saline solution shaken in bouillon and plated on blood agar. From the blood agar plates the predominating organism may be selected for the vaccine or more than one organism may be selected. Less favorable but very good results follow from inoculating and growing the washed sputum in dextrose bouillon and from this is made a vaccine consisting of all the organisms present. If the patient has a more troublesome nasal secretion or catarrhal condition of the nose and throat vaccines may be made from this source. There is a specificity among bacteria as well as among proteins in the treatment of asthmatic conditions so that if one type of organism fails to benefit other autogenous types should be tried in the form of a new vaccine. Some patients continue free from asthma for many months after vaccines are discontinued, others for only a month or two and some patients require the constant use of vaccines to be free from asthma. Succeeding courses of vaccine treatment provided that there has been no change in the bacteria which are causing the relapse seem to relieve more promptly than the first course of vaccine treatment. *When a relapse is not relieved by a second course of vaccines which previously* did relieve other bacteria should be suspected as the cause of the asthma and new vaccines should be made.

Non specific Protein Treatment

As in most chronic infections intravenous foreign protein treatment may be of benefit the same may apply to the asthmatic patient. Auld[36] reports good results from the intravenous injection of peptone. Such a procedure is likely to cause ill effects if the patient should happen to be sensitive to that or a closely related protein. Naturally non specific treatment does not throw any light on the actual cause of the disease.

Operative Measures

Operations will not benefit those who are sensitive to proteins therefore the cutaneous test should be done first. In the non sensitive cases operations on the nose and sinuses should be done only from the standpoint of seeking better

drainage in the sinuses and removing obstruction to the access of air in the nasal cavities The same applies to dentistry Of course diseased teeth tonsils adenoids and nasal spurs require removal Vaccines made from the infected areas at the time of operation are often a great adjunct and often are required to entirely clear up the infected area Operations in other localities may be of great benefit to asthmatics Babcock had an asthmatic patient with gall stones and an infected gall bladder after operation the patient was free from asthma while the gall bladder freely drained but when there was a stoppage of drainage asthma returned finally with cure of the condition asthma disappeared The author had observed a case who developed asthma soon after he developed a hernia but asthma disappeared when the hernia was repaired The same patient developed a hernia in the other groin and again asthma appeared but following repair the asthma again disappeared and has not returned. In the author s case the condition was one of asthmatic bronchitis so that probably the herniae were sufficient to lower the patient s vitality to the infecting bronchial bacteria

Climate

Change of climate does not benefit the sensitive type of patient with the exception of the pollen cases with whom the change is in reality from a place where those particular pollens are prevalent to a place where they are absent In the same way a patient may move from close proximity to a stable to a place more distant With the non sensitive or asthmatic bronchitis type of case a change of climate occasionally benefits or relieves attacks even moving for a short distance as from low ground to high ground and vice versa may relieve but such instances are not common Florida is a suitable place for an occasional case Arizona for still another California for a third and so on but no one of these states or climates is suitable for all three it is an expensive experiment and usually a bad investment

Supportive Treatment

Rarely one meets with sensitive cases and frequently one meets with non sensitive cases who do not improve under what is really the proper treatment according to experience It is these patients that require supportive treatment such as tonics rest proper diet restricted exercise fresh air and hygienic measures In such cases it is necessary to remove burdens and handicaps before the patient is able to respond to proper specific treatment

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CHAPTER VIII

HAY FEVER

BY I CHANDLER WALKER

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HISTORICAL

In 1819 John Bostock[1] first described the symptom complex of what we now know as hay fever but not until 1873 through the researches of Blackley[2] were pollens found to be the cause of the symptom In 1903 Dunbar[3] not only proved that pollens were the cause of summer hay fever but he more or less favorably treated the condition with pollens During the past ten years much work has been done by many investigators and as a result we now are able not only to recognize the cause of hay fever but we are able to treat the condition prophylactically in a very satisfactory manner

GENERAL DISCUSSION

Hay fever producing plants have in general the following characteristics they are wind pollinated are very numerous their flowers are inconspicuous and not scented and they produce large quantities of pollen Those plants which are insect pollinated and are pleasing to the eye and fragrant are as a rule not cause of hay fever whenever such flowers are suspected of causing hay fever usually it is the presence of some wind borne pollen on the flower

rather than the flower's own pollen At any rate such flowers are readily avoided whereas wind pollinated plants cannot be avoided Occasionally a highly scented flower which has little or no pollen, will produce nasal irritation which is often spoken of as hay fever but which in reality is not a true hay fever such instances will be mentioned later on Since, in general, it is the type of pollen that is spiculated or has rough outlines that most often causes hay fever it is very likely that the spicules or roughness of the pollen permits it to lodge and stay on the mucus membranes where the protein may be dissolved out and absorbed whereas smooth pollens would be more readily expelled from the mucus membranes

Scheppegrell[4] has conducted airplane experiments to determine the presence of pollen in the upper air He found that during the pollinating season of the grasses ragweeds and other common hay fever producing plants, their pollens were present in large numbers in the air up to an altitude of 4 000 feet, in diminished numbers from 4 000 to 6 000 feet and from 6 000 to 15 000 feet pollens were present in the air but in relatively small numbers Unless rain or descending air currents cause the pollens to fall pollen clouds remain in the air during the pollinating season and pollen is constantly replacing whatever should fall to earth The existence of these pollen clouds and their changes in position due to descending air currents help to explain why some patients suffer from hay fever after sunset and when a cold wind is blowing

Since the term hay fever and its synonyms as commonly used are misleading and inaccurate it is advisable to define the seasons and causes of the various varieties During April and May throughout the greater part of the United States the various trees pollinate and it is only very recently that the pollen of trees has been recognized as a cause of hay fever The next pollen season begins late in May and extends through June and more or less through July During this season the various grasses pollinate, and it is chiefly their pollen that causes hay fever at this period This type of hay fever is commonly called rose cold and is generally thought to be caused by the pollen of roses, however such is rarely the case and rose cold is a misnomer Strictly speaking it is during this season that true hay fever occurs, since it is the pollen of hay that causes the symptoms The third hay fever season begins about the middle of August and continues until the first frost usually early in October During this season the Compositae family of plants pollinates Stated briefly, therefore there are three seasons of pollen hay fever namely tree pollen hay fever in the spring grass or hay pollen hay fever in the early summer, and Compositae hay fever in the late summer or early fall

Geographical Distribution of Hay Fever Pollens

Scheppegrell[5] was the first to attempt a pollen survey and to determine the causative hay fever producing plants Although his list is a very long one the following plants he found to be of the greatest importance in the localities

mentioned Common or small ragweed (Ambrosia elatior) is the principal cause of fall hay fever east of Kansas and western ragweed (Ambrosia psilostachya) is an important cause of fall hay fever west of Kansas Giant ragweed (Ambrosia trifida) is also important east of the Rocky Mountains but not so common in New England as the small ragweed May weed (Artemisia heterophylla) is an important cause of fall hay fever in the Northwest Sage brush (Artemisia tridentata) is important during the late summer in the Rocky Mountain states as is also false ragweed (Franseria acanthicarpa) Johnson grass (Andropogon halepensis) is a common cause of early hay fever in the Middle West and poverty weed (Iva axillaris) in the Pacific and Rocky Mountain states

Causative Pollens in the East —In the New England and East Coast states no pollen survey has been made and such does not seem to be essential since the plant flora is very simple as compared with that of the South and West In New England and in the East Coast states as far south as North Carolina there are three hay fever seasons a spring season during March April and May in which the various trees pollinate an early summer season during May June and July when the grasses pollinate and a late summer or fall season during which the Compositae pollinate Of the trees the willow maple poplar and oak seem to be the chief causes of spring hay fever In the early summer period June grass is the chief cause of hay fever during May and June and timothy grass seems to be the chief cause of hay fever during June and July Although there is much red top grass and considerable orchard grass pollinating at this time treatment with timothy grass pollen seems to be sufficient and if treatment is begun early enough so that timothy treatment may be completed by the first of June there seems to be no need to consider June grass except in a rare case that has hay fever only during late May and early June In the fall it seems necessary to consider only ragweed and common or small ragweed at that as a cause of hay fever Many plants having ornamental and fragrant flowers are suspected of causing hay fever during the summer and fall but it seems fair to state that when these plants do cause hay fever it is the ragweed pollen deposited on these blossoms that causes symptoms rather than the minute sticky pollen of the plants themselves At any rate such suspected plants may easily be avoided as their pollen does not carry any distance in the air

Bernton[6] has called attention to plantain (Plantago lanceolata) pollen as a cause of asthma and hay fever This plant pollinates from early May to October in the District of Columbia and the time of profuse pollination is during the first two weeks in June Out of a series of 116 hay fever subjects Bernton proved that five or 4 3 per cent were sensitive to plantain From the author s experience it would seem that plantain is a very unusual cause of hay fever since it grows low to the ground does not pollinate very profusely but sparingly over a long period and it is encountered only in clay and damp soils it does not grow in localities like other weed The author knows of two cases in New England

Koessler and Durham[13] find that in Chicago, blue grass and orchard grass whose seasons are parallel are responsible for 80 per cent of the early summer hay fever In July red top causes some hay fever They find that in the fall small and giant ragweed are largely responsible for hay fever, and lambs quarters and pigweed are of local importance

Causative Pollens in the Middle Western States — In the following states Minnesota Iowa Missouri North Dakota South Dakota, Nebraska, and Kansas, blue grass timothy grass lambs quarters ragweeds and careless weed as outlined in the previous paragraph and in addition sage brush (Artemisia tridenda) from July to September and cocklebur (Xanthium speciosum) are important

Duke[14] finds that about Kansas City there is very little tree hay fever and of the grasses timothy blue and orchard grass are the important causes of early summer hay fever In the fall he considers short and giant ragweed marsh elder cocklebur lambs quarters water hemp and the amaranths to be the important pollens that cause hay fever

Causative Pollens in the Southern States — In the Southern States exclusive of Texas Arizona and the Southwest mountain cedar (Juniperus sabinoides) is a very important hay fever producer from December to February and cotton wood from February to April These two trees, therefore account for the longest early spring hay fever season in this country Bermuda grass which pollinates most of the year is very important as a cause of hay fever Johnson grass, which has a season from June to October is quite important During the fall in addition to Bermuda grass lambs quarters and careless weed are the most important.

SYMPTOMATOLOGY

The symptomatology of hay fever is the same no matter what particular pollen may be the cause The complaint attacks certain persons every year, and manifests itself as a catarrh of the ocular conjunctivae and of the nasal and pharyngeal mucus membranes beginning with a tickling and burning sensation, and soon consisting of marked sneezing watering and itching of the eyes and running and itching of the nose There may be much depression headache, and even marked general malaise associated with the attacks

During the attacks the mucus membrane of the nose and pharynx is highly irritable so that dust train smoke strong odors and the like aggravate the symptoms, whereas, out of season the mucus membranes are not usually affected by these mechanical irritants The length of the attack varies with the cause and depends upon the duration of pollination The pollination of trees varies from two days to two weeks of the grasses and the Compositae from six to eight weeks Occasionally the same patient has hay fever throughout two seasons each year, but the majority of persons have only the late type, which occurs from about mid August to October

Pollen Sensitization

As a result of much experimentation by many investigators we now know that most persons who have hay fever are sensitive to the protein in pollens and that whether out of season or in season those pollens when deposited upon the mucous membranes of the eyes nose or throat or injected subcutaneously into such a sensitive person cause hay fever symptoms Therefore it is proper to consider that hay fever like bronchial asthma may be a manifestation of anaphylaxis that the patient has fixed cellular antibodies and when the antigen (pollen protein) unites with its antibodies symptoms are produced It is not known why some persons are sensitive to and have hay fever from pollens when the great majority of others are not similarly affected However since patients frequently state that their first attack of hay fever appeared at a time when they were run down indisposed mentally or physically overworked or overtired and since we also know that the amount of pollen varies with the weather conditions that is in favorable years there is a bumper crop of ragweed or of hay pollen it is reasonable to suppose that either indisposition causing lowered resistance on the part of the person or exposure at some time to a tremendous amount of pollen or even more probable both conditions prevailing at the same time are the factors permitting of or predisposing to sensitization under more favorable conditions as regards the patient or less favorable as regards the crop of pollen the same individual might not and probably would not become sensitive Having once become sensitive to pollen protein very little is required thereafter to produce symptoms

Other Causes than Pollen

Although the pollens of plants cause the majority of all seasonal hay fever symptoms in a few persons whose hay fever is even limited by one or more of the pollen seasons bacteria are a cause In these bacterial cases the hay fever symptoms are not as constantly present but they are more spasmodic there is apt to be a day or two of symptoms separated by a day or two of comparative freedom Furthermore the eyes are less affected and the nose frequently feels plugged up after which there is a thick tenacious secretion rather than a thin watery discharge Such cases are usually termed spasmodic vasomotor rhinitis Infrequently the ingestion of some particular food protein is the cause of these symptoms The food proteins if they are the cause usually give a positive skin test and the bacterial protein may give a positive skin test although it usually does not as it is often the infectious element rather than the protein element in bacteria that causes the symptoms

It is not at all uncommon for some patients to complain of what they call hay fever symptoms or very frequent head colds throughout the year Since this kind of case seeks aid from the nose specialist who terms the condition vasomotor rhinitis the internist sees little of the condition and even when the

internist does not see the case first, he immediately refers the case to the nose specialist. In the future however such cases should be tested for sensitization to proteins. Not infrequently are the emanations of animals the cause of these all the year hay fever symptoms. Horsehair dandruff and cat hair are frequently the cause of these spasmodic attacks of hay fever which last a few minutes to a few hours or even a day or two, and in such instances the patient gives a positive skin test with the proteins of the hair. Less often the ingestion of various foods causes spasmodic attacks of short duration simulating hay fever. True seasonal pollen cases frequently complain of head colds throughout the year and these head colds closely simulate attacks of hay fever. In some of these pollen cases the sensitization seems to permanently render the mucous membranes extremely sensitive and irritable, so that sudden temperature changes, drafts, odors and dust particles are sufficient to produce symptoms. In other pollen cases bacteria seem to be the cause. Probably the most frequent cause of all the year round hay fever or vasomotor rhinitis from the internist's standpoint, aside from nasal abnormalities, nasal growths and sinus infections, is bacterial infection, which may be associated with the above nasal conditions or may be present alone. Naturally abnormalities of the nasal mucous membranes are frequently the cause of these symptoms of hay fever, and these abnormal mucous membranes may be due to protein sensitization, or to bacterial infection or to vascular changes. Often there is no apparent cause. However if operative procedures are not indicated such cases should be tested with various proteins to determine whether sensitization may not be the cause and even those cases which present both minor nasal abnormalities and sensitization greater benefit is offered by desensitization than by operation.

Classification of Hay Fever Cases

Therefore if all spasmodic vasomotor conditions of the nasal, pharyngeal and conjunctival mucous membrane that simulate hay fever may be as closely related as the above facts would indicate, the causes of hay fever may be schematically represented in the following table:

CAUSES OF HAY FEVER

Sensitive		Non sensitive	
Seasonal	All the year	Seasonal	All the year
tree, grass, compositae — pollen protein; food; bacterial; animal hair	animal hair protein; food; bacterial; pollen	bacterial infection	bacterial infection; vascular changes in mucous membrane of nasal cavities; abnormalities, growths and infection in nasal cavities and sinuses

Acceptance of the above classification closely correlates hay fever with bronchial asthma and in general what is written in the preceding chapter (Chapter VII) concerning bronchial asthma holds equally well for hay fever with the following exception. Seasonal pollen hay fever is extremely common whereas seasonal pollen asthma is not very usual all the year hay fever is not very commonly due to animal hair food or pollen protein as compared with the frequency of bronchial asthma that is caused by these proteins and in the non sensitive cases growths and abnormalities in the nasal cavities do not cause bronchial asthma as frequently as they do cause hay fever. Seasonal non sensitive cases of bronchial asthma which are due to bacterial infection are much more common than seasonal non sensitive hay fever which is due to bacterial infection. Seasonal sensitive food and animal hair protein cases of hay fever are about as frequent as similar cases of bronchial asthma but neither are very frequent. All the year pollen sensitive cases of hay fever and bronchial asthma are about equally prevalent and equally uncommon and all the year non sensitive bacterial cases of both conditions are very prevalent.

Comparison of Hay Fever with Bronchial Asthma

The paths through which proteins that cause hay fever enter the body are the same as in bronchial asthma namely inhalation ingestion absorption and infection the skin or cutaneous test which is used to determine sensitization in bronchial asthma is equally important and serviceable in hay fever and the kinds of proteins which cause hay fever and which should be used in the skin test are the same as those which prevail in bronchial asthma. Therefore since all of these facts have been discussed and described in considerable detail in the former chapter on bronchial asthma it is unnecessary to repeat them and the reader is referred to the preceding chapter (Chapter VII).

Pollen Tests

Tests with the whole pollen of plants may be done to find out to what type of pollen the patient is sensitive but this is not accurate as to what pollen need be used for treatment for the following reason. A patient who is sensitive to one pollen is more or less sensitive to all of the pollens in that same botanical family. Therefore when the whole pollen is tested he is apt to react to pollens to which he is not exposed. If dilutions of different strengths of a solution of the pollen proteins are tested it is usual that the patient will react to relatively greater dilutions or smaller quantities of the pollen protein which causes symptoms and to which he is usually exposed whereas with the pollens to which he is not exposed and which do not cause symptoms a stronger solution or greater amount of pollen protein is required to give a positive test. In other words a patient may give a positive test with ragweed extract in a dilution of 1-40 000 with goldenrod extract in a dilution of 1-5000 daisy in a dilution of 1-1000

and golden glow in a dilution of 1-500 Without other knowledge concerning such a patient of course ragweed pollen should be chosen as the causative agent because it reacted in the greatest dilution or smallest quantity In addition to this however it should be known to what pollens the patient is exposed and which cannot be avoided

Pollen Extracts

There are many different methods of extracting pollens for use in the tests and treatment of hay fever but the one probably most generally used is that of Clock[1] which follows The pure mature pollen grains are extracted in 66⅔ per cent glycerol and 33⅓ per cent saturated sodium chloride solution

Cooke and others use the method devised by Coca[18] which follows The dry pollens are treated with ether until all fats are removed then the pollen is extracted with the following solution sodium chloride 0 5 per cent sodium carbonate in such concentration that 10 c c of the final fluid equalled about 3 c c of tenth normal alkali and carbolic acid is added in a final concentration of 0 4 per cent

The author still continues to use the following method The dry pollen is extracted in normal saline for 24 hours then sufficient absolute alcohol is added to make a 12 per cent alcoholic saline solution and extraction is carried on for another 24 hours To the extracting fluid carbolic acid is added to make a final 0 4 per cent This alcoholic sodium chloride carbolic acid solution is used for further dilutions of the pollen protein

Pollen Treatment

The method of pollen treatment that seems to be most generally used and is used by the author is as follows It is an entirely preseasonal treatment since treatment is begun early enough ahead of the pollen season to ensure a completion of treatment just before the pollen season begins Treatment is given at weekly intervals but it may be given at five day intervals however in the writer s experience the weekly interval is preferable The first treatment is three minims or 0 1 c c of the strongest dilution that fails to give any reaction by the skin test and each succeeding treatment is an increase of two or three minims or 0 1 c c over the preceding treatment provided no reaction of any consequence resulted from the preceding treatment If at any time a treatment causes any general reaction or a local reaction larger in area than a half dollar that dose should be repeated at the next regular interval and the increase scheduled for that particular time should be postponed until the next succeeding regular interval The number of treatments necessary for any individual naturally depends upon how sensitive he may be to the causative pollen and this also depends upon how strong the stock pollen solution is and what amount of the stock solution it is desired to give the patient Therefore, since there may be

so much uncertainty it is advisable to instruct the patient to appear for tests from twelve to fifteen weeks previous to the usual onset of his hay fever thus sufficient time will be allowed for satisfactory treatment and if it happens that less treatment is required the beginning of treatment may be postponed until the proper time The importance of testing the patient with each dilution of the pollen extract with which he is to be treated is evident

Another method of treatment is similar to that described above with the exception that treatment is begun a shorter time preceding the onset of symptoms and it is continued during the period of symptoms With this method treatment is usually started six weeks before the time for hay fever symptoms to appear and treatment is continued until about the time symptoms usually disappear This method is really a combination of preseasonal and during the season treatment

A method of treatment which formerly was customary to use but which at present is not very popular is during the season treatment with no preseasonal treatment In other words treatment is begun after the onset of symptoms and is continued at three to five day intervals until symptoms disappear In conjunction with this method local treatment may be tried Estivin dropped on to the eyelids at frequent intervals seems to relieve much of the eye irritation Colored glasses benefit in that they modify the bright glaring light of the sun Mackenzie [17] has applied solutions of the causative pollen to the nasal mucus membranes on the basis that such local applications temporarily desensitize the tissues an application of the causative pollen to an abrasion of the skin as a positive reaction by the skin test does temporarily render that particular spot non sensitive

Brown [18] uses the following method of during the season treatment with considerable success He gives a dose of the weakest solutions every day the next strongest solutions every other day and so on in other words as the dose of pollen extract was increased the interval betweeen doses was lengthened

Duke [19] has recently originated a short interval treatment He begins treatment usually about four weeks before the onset of symptoms and continues the treatment practically throughout the season of pollination The injections are given twice daily in the beginning of treatment and the dose is doubled at each inoculation until the stronger dilutions are reached when it is frequently necessary to omit one of the daily injections or even to allow a two or three day interval between treatments During the latter part of treatment an interval of three or four days is allowed between injections He does not repeat a dose until the local effect of the previous one has subsided and he does not increase a dose if the previous one caused any constitutional reaction

Results of Treatment

It is quite impossible to give absolute statistics as to the results of hay fever treatment because there is no uniformity in the classification of results or the

method of making the pollen extracts or the method of giving treatment. The following are some statistics which are available and which will give a general idea as to the results obtained from preseasonal treatment. Vander Veer[9] obtained complete relief in 25 per cent, marked relief in 49 per cent, slight relief in 18 per cent, and no relief in 10 per cent of a large series of cases. Rackemann[1] obtained complete relief in 9 per cent, considerable relief in 62 per cent, and no relief in 8 per cent of a series of 91 cases. Piness[22] in a series of 202 cases reports 29.6 per cent complete relief, 40.1 per cent obtained great relief, 21.4 per cent were at least 50 per cent benefited, and 9.1 per cent received no benefit.

The author during the past three years has obtained the following averages: complete relief in 10 per cent, practically complete relief in 24 per cent, at least 75 per cent benefit in 3 per cent, at least fifty per cent benefit in 28 per cent, and no benefit in 6 per cent.

It seems to be the consensus of opinion that preseasonal treatment for hay fever offers by far the best results for the ensuing season and probably it is the only method so far developed that offers much for permanent relief. There are no statistics available to show that permanent relief may be obtained, but the author has learned that of the patients that he had treated preseasonally during the years 1918, 1919, 1920, 1921 and 1922, twenty per cent have been free from symptoms without treatment ever since. Another 8 per cent were able to omit treatment one or two years without symptoms, after which symptoms gradually returned, and another 8 per cent who omitted treatment one year had as much hay fever as previous to treatment. The fact that twenty per cent have probably been cured and another eight per cent were able to skip treatment one or more years would seem to be strong evidence in favor of preseasonal treatment.

Next to preseasonal treatment the combination of more or less preseasonal with during the season treatment seems to offer the best results. Treatment given only during the season offers less benefit and no permanent relief, but it is worth trying for a few doses as some patients get considerable benefit. Any physician who specializes on hay fever will naturally use all of these methods. He will desire and attempt to give entirely preseasonal treatment, but the later the patients apply for treatment the less preseasonal and the more during the season treatment will have to be used, and some will apply so late that during the season treatment must be tried.

Duke's method of treatment evidently is not available to physicians in general as he makes the following statement in regard to his methods: "The above plan of treatment (meaning his own method) is not recommended to physicians who are not thoroughly experienced in the use of pollen because of the fact that if technique is imperfect pollen reactions can be severe, alarming and dangerous."

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CHAPTER VIII A

SYNCOPE AND RELATED SYNDROMES

By SOMA WEISS

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Introduction

There are few acute clinical manifestations which present a more alarming and more dramatic picture than syncope Although it is a common condition

little has been known of its nature and etiology, notwithstanding the fact that several volumes were written on the subject in the eighteenth and nineteenth centuries Until very recently we could repeat what Gowers[1] said in 1907 " Familiar as fainting is, adequately as we seem to know it, there is much in it that we do not know Our knowledge is enough to obscure our ignorance "

It is difficult to give a satisfactory definition of syncope which describes its main features and distinguishes it from attacks which are quite similar in appearance but differ in their pathogenesis and prognostic significance Syncope is an acute and usually transient bodily state characterized primarily by a sudden and unexpected partial or complete, suspension of the functions of locomotion consciousness and often of circulation and respiration It occurs as will be shown presently as a result of different bodily and mental states, and therefore should be considered as a syndrome with varying etiology The manifestations associated with syncope are many and include a number of the bodily functions regulated by the vegetative nervous system In addition to the classical type of syncope there are frequently present equivalent milder manifestations which may be termed *syncope variants* The physiologic mechanism underlying the clinical manifestations of syncope varies in different types of syncope and the details of the pathogenesis will be discussed under separate headings

An analysis of oo unselected cases with a presenting picture of syncope recorded in the Boston City Hospital revealed that in the great majority of instances no organic disturbances of the body were present Clinical study of these patients indicates that fainting resulted most frequently from an abnormal state of the central nervous system and from prolonged standing In a smaller proportion of the cases such organic diseases as arterial hypertension, cerebral and coronary sclerosis, mitral and aortic stenosis bore a relationship to the syncope

The prognostic significance of syncope like the etiology shows great variation In the majority of instances prompt recovery follows and the attacks are consistent with longevity and with general good health at times however syncope may be fatal In many instances an attack of syncope arouses the fear of ' heart disease on the part of the subject and it is for this reason that physicians often are consulted

The classification of syncope to be presented here cannot be considered entirely satisfactory or final The separation of the groups is not based on uniform criteria although usually the underlying physiologic mechanism has been taken as the basis of the grouping Transitional types of syncope are also common The presentation of the subject as described here nevertheless represents a definite advance when compared with the knowledge of the subject in the past Thus while as early as 1768 Boissier de Sauvages on the basis of symptoms of doubtful significance differentiated twenty one types of syncope during the

past few decades the interest in this subject has lagged and no attempt has been made to separate the types of syncope on the basis of the underlying mechanism.

Present knowledge justifies the separation of the following types of syncope

Types of Syncope

Vasovagal Syncope (*Common Fainting Attacks*)

This is the most common type of syncope. The term vasovagal syncope is used here as applied by Lewis[3] although Gowers used the term earlier for the designation of an entirely different type of transient attack. In order to avoid confusion this latter condition should be termed Gowers syndrome and not vasovagal syncope as there is no evidence indicating that in Gowers syndrome the vagus is involved. In vasovagal syncope on the other hand a marked degree of vascular change as well as of vagal inhibition occurs. The term "common fainting" may be properly applied to this type of syncope because it occurs more frequently than all other types combined.

In the group of vasovagal syncope belong the majority of the fainting attacks which occur as a result of prolonged standing particularly in persons with poor muscular tonus and the fainting attacks which develop under emotional stress. The large number of persons who collapse while watching the parade usually suffer from vasovagal syncope. The mechanism underlying the syncope observed in patients after prolonged bed rest or in patients with effort syndrome is in many instances that of vasovagal syncope. This type of syncope occurs in both sexes particularly at early adult age. While in general poor physical health, chronic undernutrition and anemia are predisposing factors attacks not infrequently occur in robust healthy persons. They usually develop while the patient is standing and seldom while he is recumbent. Fatigue, fasting, mental worry or conflict, pain, emotional tension in general, confinement in a crowd or in an overheated and poorly ventilated room, straining during defecation or the administration of an enema may act as precipitating or contributory factors singly or combined. A hot bath or hot shower may bring on an attack particularly if taken when the bodily state and the vasomotor tonus are altered by other factors such as gastrointestinal disturbance and mild infections. Suggestion may also have a role in precipitation of the attack. Thus it is not a rare experience of physicians performing routine vaccination of a group of subjects to find that following the occurrence of syncope in one of the subjects several members of the group who follow and who observed the attack will faint also. The appearance of the subject while in such a faint, the behavior of the blood pressure and the heart rate indicate that we are dealing with vasovagal syncope

little has been known of its nature and etiology, notwithstanding the fact that several volumes were written on the subject in the eighteenth and nineteenth centuries Until very recently we could repeat what Gowers[1] said in 1907 ' Familiar as fainting is adequately as we seem to know it, there is much in it that we do not know Our knowledge is enough to ob cure our ignorance "

It is difficult to give a satisfactory definition of syncope wh ch describes its main features and distinguishes it from attacks which are quite similar in appearance but differ in their pathogenesis and prognostic significance Syncop is an acute and usually transient bodily state characterized primarily by a sud den and unexpected partial or complete, suspension of the functions of locomotion consciousness and often of circulation and respiration It occurs, as will be shown presently as a result of different bodily and mental states, and there fore should be considered as a syndrome with varying etiology The manifesta tions associated with syncope are many and include a number of the bodily func tions regulated by the vegetative nervous system In addition to the classical type of syncope there are frequently present equivalent milder manifestations which may be termed *syncope variants* The physiologic mechani m under lying the clinical manifestations of syncope varies in different types of syncope and the details of the pathogenesis will be discus ed under separate headings

An analysis of oo unselected cases with a presenting picture of syncope re corded in the Boston City Hospital revealed that in the great majority of instances no organic disturbances of the body were present Clinical study of these patients indicates that fainting resulted most frequently from an abnormal state of the cen tral nervous system and from prolonged standing In a smaller proportion of the cases such organic diseases as arterial hypertension cerebral and coronary scle rosis mitral and aortic stenosis bore a relationship to the syncope

The prognostic significance of syncope like the etiology, shows great varia tion In the majority of instances prompt recovery follows and the attacks are consistent with longevity and with general good health at times however syncope may be fatal In many instances an attack of syncope arouses the fear of ' heart disease ' on the part of the subject and it is for this reason that physicians often are consulted

The classification of syncope to be presented here cannot be considered en tirely satisfactory or final The separation of the groups is not based on uniform criteria although usually the underlying physiologic mechanism has been taken as the basis of the grouping Transitional types of syncope are also common The presentation of the subject as described here nevertheless represents a definite advance when compared with the knowledge of the subject in the past Thus while as early as 1768 Boissier de Sauvages on the basis of symptoms of doubtful significance differentiated twenty-one types of syncope, during the

movements localized over the facial muscles or over the upper part of the body in rare instances they may be generalized There is no other condition including the deepest coma which so closely resembles death No wonder that a simple benign syncope is often described as an attack in which the patient almost died and contrariwise that some cases of instantaneous death are believed at first to be but fainting

The moments during which this vital differential diagnosis has to be made are anxious ones even for the most skilled and most experienced physicians This differentiation is made more difficult by the fact that not infrequently the aura of a rapidly approaching vasovagal syncope may be identical with that of a serious or fatal cardiac seizure Thus an unexplained anxiety or a feeling of impending dissolution angor animi or the angor molestus of Morgagni may precede this type of syncope just as it does angina pectoris or coronary thrombosis I have seen instances of severe vasovagal syncope following the administration of vaccine or of serum which have been mistaken for an acute and unusual anaphylactic reaction in which the patient almost died The duration of unconsciousness varies from a few seconds to several minutes The rate of recovery from severe attacks usually is slower than the rate of onset Nausea involuntary or voluntary micturition or defecation profuse perspiration together with the improvement of the heart sounds and the increased force of the pulse may be early indications of recovery Partial consciousness may return promptly often with a short period of disorientation Gradually the muscular power and coordination return but often the patient remains pale perspiring limp and inert for from one half hour to an hour Headache anorexia and weakness may last for from twelve to twenty four hours or longer Laceration of the skin fracture of the skull and other bones are not uncommon results of the fall

The attack frequently comes on gradually and when this is the case a more careful analysis of the clinical manifestations of the onset is possible Such a study can be made as we have done[8] on voluntary subjects having a tendency to vasovagal syncope who have been placed on a tilting table or on subjects given from 0 06 to 0 2 gm of sodium nitrite and placed on the tilting table The observations made on such subjects as well as those made on patients subject to spontaneous attacks indicate that the attack often does not reach the stage of motor collapse and unconsciousness but ceases at an early stage representing forme fruste manifestations of syncope Frequently the patient collapses but remains vaguely aware of his surroundings The premonitory manifestations of an attack with slow onset often consist in a peculiar feeling over the epigastrium or over the heart and in a sensation of weakness associated with giddiness and light headedness At times there may be a throbbing headache with ringing in the ears or severe pain over the heart Yawning abdominal cramps

Some persons faint whenever they develop vomiting from whatever cause The syncope which is relatively common in pregnancy particularly during the first four months is also vasovagal in type Some persons during pregnancy develop rather pronounced hypotension and instability of the vasomotor system These states then are accentuated further by the frequent attacks of nausea and the emotional state of the nervous system The syncope of mountain sickness also has all the characteristics of vasovagal fainting

In some of the vasovagal syncopes such as develop during instrumentation the precipitating factors may be a combination of emotional strain pain and reflex stimulation Such instances are well known to every physician Sir Astley Cooper describes an instance of such syncope "A person has a bougie passed into his urethra for the first time the urethra is irritated by it he says I feel faint becomes sick looks pale and without care, he drops at your feet his pulse has nearly ceased and his body is covered with a cold perspiration You place him on a sofa with his head a little lower than his body, and as soon as the blood freely enters the brain all his functions are restored

Vasovagal syncope occurs also in patients with organic disease Some of the attacks in such patients however are independent of the organic disease On the other hand there are organic diseases in which the vasovagal type of syncope occurs relatively frequently and in which a causative relationship exists Infectious diseases with fever mitral and aortic stenosis congenitally narrow aorta open ductus arteriosus arterial hypertension with fluctuating pressure and aortic regurgitation are some of the conditions which apparently predispose to the attack Syncope that occurs during or immediately after the removal of a large *amount of abdominal fluid is vasovagal in nature Syncope under the* latter condition is more apt to occur if the patient is in the sitting rather than in a recumbent position

Administration of vasodilator substances particularly those acting on the splanchnic area is apt to produce characteristic vasovagal syncope Thus the sudden syncope following the administration of nitrites is identical in every respect with vasovagal syncope Certain attacks of syncope observed in the course of spinal anesthesia also belong in this group

Clinical manifestations may *show considerable variation depending* on the rate of onset of the attack In the severe type with rapid onset the patient collapses instantly without warning The body lies crumpled and motionless The face and the body surface are ghastly pale The pupils usually are dilated and the conjunctival reflexes are absent Respiration usually is either shallow and slow or deep and sighing The heart sounds are slow or normal in rate barely audible The radial pulse may be imperceptible or weak but the carotid and femoral pulsations usually are easily palpable There may be rather slow, clonic

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associated with markedly accentuated peristaltic sounds, periodic waves of nausea and severe belching frequently are present The duration of these symptoms may vary considerably Some patients just before they collapse experience a sensation of coldness or numbness starting at the lips or the fingers and toes and moving toward the heart The transition from these early manifestations to the point of unconsciousness and collapse is either gradual or very rapid From the point of view of differential diagnosis it is of interest that as a rule, there is no sense of rotation or of objects surging before the eyes, which is a common manifestation of auditory vertigo

Mechanism — There are three types of changes observed in vasovagal syncope which bear on the underlying changes in the hemodynamics The subject is always pale with collapsed superficial veins the pulse pressure is low, and during and just preceding the onset of unconsciousness there is frequent but not always marked slowing of the cardiac rate That the slowing of the heart rate is the result of vagal tonus is shown by the fact that atropin in doses of from 1 to 2 mg injected subcutaneously abolishes the cardiac slowing but seldom prevents the onset of syncope Thus the cardiac slowing is not a causative but at most only a contributory phenomenon[3] The fall in the blood pressure develops independently of changes in the cardiac rate Indeed there are spontaneous attacks of vasovagal syncope without cardiac slowing but rather with continuously increasing heart rate

Thus the changes regularly present in vasovagal syncope are a fall in the pulse pressure resulting either from lowered systolic or from elevated diastolic blood pressure and an emptiness of the superficial veins of the neck and veins of the skin indicating a lack of return blood flow That the cardiac output is actually decreased preceding and during the syncope is indicated by the observation of Turner[8] who has studied the adjustment of heart rate and arterial pressure in healthy young women during prolonged standing Turner noted that those subjects whose cardiac output fell off most markedly on standing motionless often were the ones who gave evidence of lessened circulatory efficiency by fainting dizziness or a sense of extreme fatigue It was also noted that in this group of subjects the diastolic pressure rose progressively on standing until the pulse pressure was very low and that in this state dizziness and later fainting occurred It appears that during standing the muscular and abdominal massage is lacking in such subjects Starr and Collins[9] measuring with ethyl iodid the blood flow of subjects in a standing position just before or at the beginning of the sensation of faintness observed no reduction in the cardiac output These subjects, however, showed no changes in arterial pressure hence it is questionable whether the findings can be interpreted as bearing on vasovagal syncope

We have observed in subjects kept motionless on a tilting table under standard

conditions marked variations in the tendency to faint The symptoms and signs exhibited by the subjects as well as the underlying circulatory mechanism correspond in every respect to those observed in patients with spontaneous va o vagal syncope We have also noted that the tendency to faint can be increased by the administration of from 0 06 to 0.. gm of sodium nitrite In some instances such amounts of sodium nitrite produce no appreciable change in the arterial pressure while the subject is in the horizontal position but fainting promptly oc curs when he assumes an upright position

The relation of symp oms to alterations in the cardiovascular system in va o-vagal syncope is be t illustrated by the ob ervations made on the following subject

A 7 year old subj ct w ho suffered from no organic di ease had a heart rate of 8 per minute and an arterial blood pressure of 106/36 mm Hg when in th horizontal position on the tilting table The position of the tilting table was changed gradually in the cour e of twenty minutes to an angle of 80 degrees at the same time the heart rate ro e to from 110 to 114 per minute and the arterial pressure changed to an average level of 110/74 The patient felt somewhat drowsy and sighed and yawned frequently He was then returned to the horizon tal pos tion and was given 0 15 gm of sodium nitrite orally This amount of sodium nitrite induced no appreciable change in the arterial pressure while the patient was in the horizontal position Ten minutes after the administration of the nitrite the tilting table was raised to an angl of 50 degrees The heart rate was then 114 per m nute and the arterial pressure 78/54 mm Hg The patient experienced a heavy sen ation over the stomach Fifteen minutes after starting th tilting when the table was at an angle of 66 d grees the heart rate rose to 1 8 per minute and the arterial pressure was 78/60 mm Hg The pa ti nt was nau eated and belching Eighteen minutes later when the angle of 80 degrees was reached the heart rate rose to 140 per minute and the arterial pressure wa 58/56 The patient became pale the radial pul e was barely palpable he complained of weakness and fa nted Th blood pre sure could not be measured and the electrocardiogram indicated that the heart suddenly slowed to a rate of 55 per minute The lowest rate as obtained through auscul tation was 38 The tilting table was changed instantly to the horizontal position The patient remained unconscious for about one to one and one half minutes exhibiting coar e tremor all over the body thereafter he retched and woke up with complete amnesia for the immediate past He was pale the skin was cold and covered with beads of per piration One minute after he was returned to the horizontal position the heart rate was 70 and the arterial pressure 96/50 mm Hg Four minutes later the heart rate was 83 and the arterial pressure 102/56 indicating that in the horizontal position the heart rate and the arterial pressure returned to normal in spite of the admini tration of sodium nitrite (Fig 1)

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a result of vagal inhibition As indicated by the clinical manifestations it is probable that in vasovagal syncope a number of functional changes in the autonomic nervous system play an important role but this aspect of the problem has yet to be investigated

In the majority of instances of vasovagal syncope the instability and particularly *the decreased tonus of the splanchnic vascular system are important factors* Such instability as has been shown may be a permanent constitutional characteristic it may be the result of prolonged rest in the recumbent position it may be caused by bacterial toxin or other chemical substances or it may be a temporary nervous phenomenon of psychic or neurogenic origin as for example in patients who faint following a prolonged period of nausea It is known that nausea and vomiting are primarily reflex acts and that the efferent mechanism of the reflex is widespread, involving numerous changes in the functions of the gastrointestinal respiratory and cardiovascular systems A reflex fall in blood pressure and a decreased return of blood are among the regular accompanying manifestations These changes may reach such a degree that fainting ensues Similarly, the syncope or the milder manifestations observed after sudden removal of a large amount of ascitic fluid depend primarily on the sudden relaxed state of the splanchnic vascular areas

Although these examples suggest that vasovagal syncope depends mainly on splanchnic dilatation the exact mechanism of the changes is not known it is certain however that in addition to the mechanical factors reflexes are also active Similarly the nature of the vagal inhibition is not clear at present Experimental evidence is available indicating that the vagal centers are particularly sensitive to the stimulating effect of sudden cerebral anoxemia

The circulatory changes preceding and during syncope are not unlike those observed in peripheral circulatory failure or in shock Vasovagal syncope may indeed be looked upon as an acute and transient circulatory collapse It is of interest that between attacks these patients often show no abnormal variations in the arterial pressure on changing from the horizontal to the upright position Similarly the response to stimulation of the carotid sinus and other cardiovascular reflexes is normal

It is a common belief that vasovagal syncope is always a transient and hence a benign manifestation Obviously at present the term is used to define only such a transient collapse Clinical observations however strongly suggest that in certain states of the body attacks with identical mechanism may have a fatal outcome Such is apparently the case in instances of sudden almost instantaneous death occurring particularly in elderly patients with coronary arteriosclerosis who collapse on getting out of bed after a prolonged period of rest and die without warning Postmortem examination in these cases fails to reveal

These observations show the effect of posture on the heart rate and on arterial pressure when the usual orthostatic adjustments are disturbed. They demonstrate the symptoms and signs associated with a progressively falling pulse pressure *superimposed on a rising diastolic pressure. It is also clear that the* cardiac inhibition followed a marked rise in the heart rate just before fainting occurred.

Thus we believe that in the mechanism of vasovagal syncope the most significant and most constant change is the progressive decrease in the pulse pressure usually associated with an elevated but sometimes with a normal or even a decreased diastolic pressure. The changes in the pulse pressure and the rise in the diastolic pressure in particular observed before the onset of symptoms, may well depend on a certain adjustment response of the vessels to stagnation of blood in the splanchnic and other vascular areas. Simultaneously with these changes

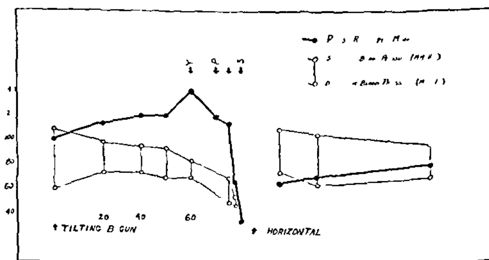


Fig. 1.—Changes in the arterial pressure and heart rate before, during and after a vasovagal syncope induced by tilting and administration of sodium nitrate. *Note the progressive decrease of the pulse pressure and elevation of heart rate.* The latter fell rapidly just before and during fainting from a rate of 140 to 38 per minute. *Note the rapid return of the arterial pressure to normal after the body was brought back to the horizontal position.*

there is a decreased venous return of blood. During such a state, which may last for varying lengths of time, the heart rate usually is elevated. When finally a point is reached where the pulse pressure is very small or imperceptible, syncope follows. Practically simultaneously with the onset of fainting both the systolic and diastolic pressures fall so rapidly that often the blood pressure cannot be recorded. It is in this stage that sudden cardiac slowing develops as

the lack of cultivation of physical training among women, and finally the prevalence of chlorosis must have been significant predisposing factors which in recent decades play but a small role

Treatment — Effective preventive measures depend entirely on the predisposing cause or causes in the individual case If emotional factors play the primary role an intelligent psychic approach improves the stability of the vasomotor system Massage physical exercise and proper postural and breathing habits may result in more efficient return of blood to the heart and hence may lessen the tendency to faint Abdominal supports may prove effective Some patients should be instructed not to stand motionless but rather to move the weight of the body rhythmically from one leg to the other After prolonged bed rest patients should be instructed to change the position of the body from recumbent to upright slowly The better knowledge of vasovagal syncope lends support to the importance of careful supervision of patients when they are allowed to get out of bed If anemia is present this should be rectified It is also advisable to instruct patients having a tendency to faint to sit or lie down whenever premonitory symptoms appear

The management of patients with vasovagal syncope consists in the prompt application of a few simple measures The body should be placed at once in a horizontal position with the head lowered The clothing should be loosened or removed The face should be rubbed with ice water Inhalation of ammonia or other olfactory stimulants is helpful Epinephrin may be injected intravenously in doses of 1 c c (15 minims) of a solution of 1 10 000 (a ten times diluted stock solution of 1 1 000) Subcutaneous administration is not rational because of the poor absorption under such conditions Inhalation of a mixture of 10 per cent carbon dioxid and 90 per cent oxygen may be helpful In a few instances I have seen instantaneous recovery from vasovagal syncope following the intravenous administration of from 1 to c c of coramin In desperate cases artificial respiration and cardiac massage are indicated After the return of consciousness the patient should be left in a comfortable horizontal position until normal or almost normal muscular power has returned For the post syncope headaches the commonly used analgesics are beneficial

Carotid Sinus Syncope

The carotid sinus is the slight bulbous dilatation at the bifurcation of the common carotid artery (Fig 2) This bulbous dilatation involves mainly the origin of the internal carotid artery It has been shown particularly by de Castro[7] and by Sunder Plassmann[18] that the carotid sinus is richly supplied with sensory receptor nerves terminating in characteristic menisci These

coronary thrombosis or other changes which might adequately explain the cause of death As the presence of coronary sclerosis often is associated with an increased tendency of the heart to vagal inhibition, this factor, together with the unstable and weak vasomotor tonus resulting from prolonged bed rest, may lead to such a severe degree of pooling of blood in the periphery, and to such a prolonged inhibition of the cardiac function during syncope, that recovery of adequate circulation is impossible Such a situation is particularly apt to arise when the patient is propped up in a wheelchair or in an armchair Under such conditions during fainting the body cannot assume a horizontal position and recovery of a normal venous return is so impeded that dangerous cerebral ischemia rapidly results Whenever death is truly instantaneous it has been my experience that postmortem examination usually disproves the existence of coronary thrombosis of cerebral vascular accidents or of pulmonary infarcts which are the erroneous diagnoses usually attached to such sudden and unexpected fatal accidents It is of interest that as early as 1740 Hoffmann[10] described patients suffering from otherwise benign diseases who developed a severe degree of collapse on standing at times with fatal outcome Liebermeister[11] in 1864 called attention to the frequency of sudden death during defecation among chronic invalids on first getting out of bed and he attributed such accidents to changes in the circulation related to the upright position of the body These early clinical observations have not been controlled by means of autopsy findings hence we cannot be certain of the underlying conditions It is of interest nevertheless that the significance of vasomotor weakness and upright position of the body were appreciated by some of the physicians of the distant past

Such considerations give a rational basis for the popular belief that fright may be responsible for death particularly in the presence of coronary disease Among patients with angina pectoris death from emotional causes is not rare

The *frequency* of vasovagal syncope varies considerably In some subjects fainting occurs but once in their lifetime in others it recurs at irregular intervals There are persons in whom there is an increasing tendency to faint The reactions of such patients suggest that the syncope behaves like a conditioned reflex inasmuch as after repeated faintings less and less emotional strain may result in the discharge manifestations of syncope Thus recent advances in psychophysiology establish a physiologic basis as well as a certain "justice" for the behavior of some of the more sensitive ladies of the Victorian era

The high frequency of syncope in the remote past as judged also from numerous references in the literature and from illustrations in fine arts may be due to a number of causes other than that just mentioned The tight corsets worn not only by women but also by men which must have seriously interfered with the venous return as well as with the proper function of the diaphragm

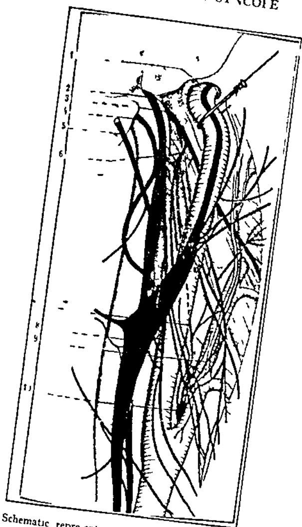


FIG 3 — Schematic representation of nerve structure in and around the carotid sinus (Hovelacque Maes Binet and Gavet Presse Médicale 1930 1 451) (1) the carotid fiber of the sympathetic nerve along the artery (2) the vagus nerve (3) the glossopharyngeal nerve (4) the spinal nerve (5) the hypoglossal nerve (6) anastamosing branch between the glossopharyngeal and vagus nerves (7) the intercarotid nerve a branch of the glossopharyngeal nerve (8) the superior cervical sympathetic ganglion (9) a branch of the intercarotid nerve ending partly in the carotid body partly in the intercarotid plexus (10) the carotid body (Courtesy of Presse Médicale)

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menisci, particularly rich in the adventitia, emerge from the sinus as the sinus nerve of Hering or the "intercarotid nerve of de Castro" This nerve was known to the old anatomists as 'ramus caroticus hypoglossi' or as ramus descendens hypoglossi its significant physiologic and pathologic functions however have become known but recently mainly through the contributions of Hering[14] and Heymans[1] (Fig 3) The intercarotid nerves together with the aortic depressor nerves represent the most important or perhaps the sole



Fig 2 —The appearance of the bulbous dilatation of the internal carotid artery—the carotid sinus in man (Courtesy of Medicine)

reflex regulatory mechanism of the blood pressure In addition the carotid sinus nerves exert a significant influence on the vagus system in general, and on the cardiac inhibitory endings in particular They also exert a reflex influence on the functions of a number of other organs including the adrenal glands

The evidence at present available suggests that the regulatory function of the carotid sinus reflex becomes particularly active under physiologic stress Under such circumstances the tonic impulses travelling through these nerves tend to prevent undue elevation of the arterial pressure and increase in the heart

from a direct reflex fall in the arterial pressure occurring independently of any change in the heart rate This reflex is a carotid sinus vasodepressor reflex The fall in arterial pressure depends on a reflex dilatation of peripheral vascular areas *In contradistinction to the first group atropin exerts no influence on the* attacks but they may be abolished by epinephrin and other vasopressor sub stances which counteract the vasodepres or effect of the reflex

The manifestations observed in both these groups can be explained to some extent on the basis o generalized cerebral ischemia It ha been pointed out by

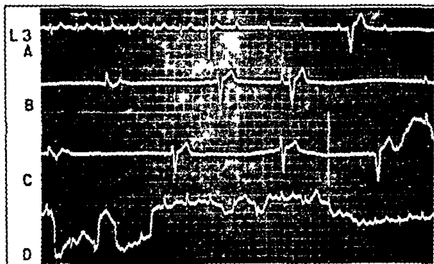


FIG 4 — P olon ed a y tole with ynope and convul ions in luced by mechani al pres ure on the carotid inus Electrocard o ram lead III A B C and D repre ent continuous tracing The vertical white lines in A and C indicate b ginning and end of firm pre sure on the carotid inus *Note block ventricular escape and bizarre Q R S T* complexes The wavy tracing in C and D indicat a onvul ion with recovery at the end of D (Courtesy of Medicine)

Weiss and Baker[1] however that the dominant role is played not so much by the absolute degree of cerebral ischemia as by the rate of change from the normal state to an ischemic state

In the third group of cases the clinical manifestations are identical with or similar to those in the other groups and stimulation of the carotid sinus promptly induces a state of unconsciousness although neither cardiac slowing nor fall in the blood p essure precedes or accompanie the attacks Neither atropin nor epinephrin has any effect on the attacks It is a remarkable fact that in spite of the absence of demonstrable changes in the systemic hemodynamics the in

rate They also exert a balancing influence on a number of midbrain centers, counteracting particularly the overactivity of certain sympathetic functions[16]

Clinical and experimental evidence indicates that the carotid sinus reflex may become abnormally hyperactive in man, and as a result, it may be responsible for syncope and related manifestations The evidence which Baker, Capps Ferris and I[1 18] have gathered indicates that such hyperactivity of the carotid sinus reflex may result from hyperirritability of the nerve endings within the sinus from hypersensitivity of the synapses of the center, or from irritability of the end organs of the reflex alone or in combination In the light of present clinical experience, the underlying morbid changes influencing the reflex consist in organic lesions such as inflammation enlarged lymph nodes malignant tumors in the neck arteriosclerotic aneurysmal dilatation of the sinus or sclerotic alterations in the coronary vessels and in the conductive system Hyperactivity of the reflex may be induced by chemical agents or by nervous hypersensitization such as occurs following the administration of digitalis or in certain emotional states

The evidence that hyperactivity of the carotid sinus may result in syncope and related manifestations is based (*a*) on observations of spontaneous attacks in a number of subjects (*b*) on the history and character of the precipitating factors (*c*) on the fact that mechanical stimulation of the carotid sinus promptly induces syncope identical in nature to that of the spontaneous attacks (*d*) on the observation that occlusion of the carotid artery below the sinus fails to cause similar symptoms indicating that simple cerebral ischemia resulting from arterial occlusion is not involved (*e*) on experiments showing that when the hypersensitivity of the sinus is unilateral, stimulation of the normal sinus is not associated with syncope (*f*) on the observation that novocain block of the sensitive sinus abolishes all induced reactions and (*g*) on the results of denervation of the carotid sinus which in 10 cases abolished both spontaneous and induced attacks

A closer study of the underlying mechanisms in syncope of carotid sinus origin permits the division of this type of syncope into three groups In the first group the syncope and related symptoms depend mainly on a reflex vagal inhibition of the heart and a fall in the arterial pressure which depends on the cardiac slowing Depression of the sensitivity of the cardiac motor endings of the vagus by means of atropin abolishes the cardiac slowing and consequently the attacks of syncope Epinephrin and ephedrin by increasing the irritability of the myocardium also prevent the occurrence of long asystoles and hence abolish the attacks Obviously this type of syncope may be looked upon as a special form of Adams Stokes attack of reflex origin the latter being a carotid sinus cardioinhibitory reflex (Figs 4 and 5)

In the second group of cases the spontaneous and induced attacks result

first two groups were however somewhat older than those in the third group and in those in the first group coronary sclerosis seemed to be an important etiologic factor In the third group an imbalance of the autonomic nervous system was present relatively often

Hyperactivity of the carotid sinus reflex is present as a rule without hyper activity of other autonomic reflexes which may be responsible for syncope and conversely patients who suffer from vasovagal syncope syncope caused by postural hypotension or vagovagal syncope do not exhibit overactive carotid sinus reflexes

The type of reflex cardiac irregularity associated with the cardiac slowing varies Simple sinus bradycardia sinoauricular block partial or complete au riculoventricular block complete asystole and short periods of ventricular fibrilla tion have been observed

The fact that attacks can be induced with regularity by stimulation of the carotid sinus affords an excellent opportunity to study the clinical manifesta tions in detail Naturally these manifestations vary with the intensity and the duration of the stimuli The state of unconsciousness often is preceded by aurae such as epigastric discomfort ringing in the ears or visual hallucinations If stimulation of the sinus is maintained the state of uncon ciou n ss i fol owed soon by convulsive movements Such movements usually tart over the con tralateral side but often they are generalized

In the precipitation of spontaneous attacks various factors are contributory In some instances sudden turning of the head usually toward one side or to the side and upward induces attacks Thus in the case of a street car motorman who wore a high stiff collar sudden turning of the head frequently caused syncope and abandoning the stiff collar resulted in cessation of the attacks Administra tion of digitalis particularly in elderly patients with coronary di ea e some times results in increased sensitivity of the carotid sinus reflex and in attacks of syncope In younger persons with hyperactivity of the inus emotional fac tors play a definite role in the sensitization of the reflex In many cases of hyper ensitive carotid sinus reflex with spontaneous attacks of syncope how ever the history does not yield adequate information to permit drawing con clusions regarding the precipitating factors It is probable that the efficacy of the knock out from a blow on the jaw depends on the stimulation of the carotid sinus reflex and on the resulting cardiovascular changes

The frequency and intensity of attacks vary in different subjects In some cases the intervals between attacks are irregular In female patients there is a tendency for the attacks to recur at the time of the menstrual periods Sys tematic tests over a prolonged period revealed periodic fluctuations in the sensi tivity of the reflex[17 18]

duced attacks appear at times within three to four seconds after stimulating the sinus, in contrast to from twelve to sixteen seconds in cases of the first group with complete cardiac standstill. This finding, together with the results of comparative measurements of the cerebral blood flow in subjects during and between attacks and with the results of pharmacodynamic observations, indicates that alterations in the general cerebral blood flow play no part in the precipitation of symptoms in this group. The study conducted on such subjects by Ferris, Capps and Weiss[1], as well as certain data available from experiments

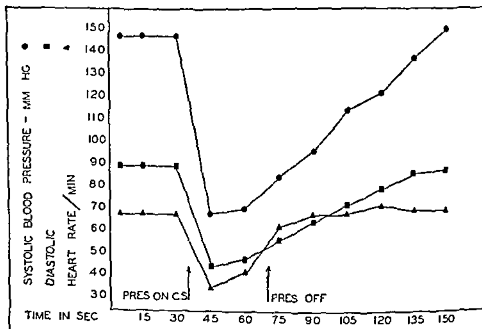


FIG. 5.—The effect on heart rate and blood pressure of stimulation of the carotid sinus in a hypersensitive subject suffering from syncope. Note that both heart rate and blood pressure show a marked fall immediately after stimulation of the sinus. When the pressure is released the heart rate returns to normal quickly, the blood pressure more slowly. (Courtesy of Medicine)

on animals leads to the conclusion that in the induction of attacks in the third group designated as the "cerebral type of syncope," nervous impulses from the sinus act on a center or centers in the midbrain, the function of which is the regulation of consciousness. Whether the nervous impulses travelling through the intercarotid nerves act directly on these centers or indirectly through local vascular changes cannot be stated on the basis of the available evidence.

Among the patients whom we have observed, the *clinical manifestations* have been practically identical in the three types of fainting. The patients in the

fusion or unconsciousness During the attack, the face is pale Some patients appear "as if dying" Depending on the activity of the type of reflex or reflexes the heart rate may be slow or normal and the pulse imperceptible weak or normal Immediately following the attack the face becomes flushed and there is profuse perspiration Hyperpnea of varying degrees and at times dyspnea precedes the syncope in some instances

In no instance have we observed that induced attacks harm the patient nor do we know of any case with spontaneous seizures in which death was instantaneous or which suggested that hyperactivity of the carotid sinus reflex might be responsible for death We have refrained from simultaneous bilateral stimulation of the carotid sinus As pointed out by Ferris Capps and Weiss [9] the only evidence that manipulation around the carotid sinus may lead to dangerous syncope or to death is the occurrence of instantaneous death during the administration of volatile anesthetics particularly following digitalization Digitalis has a definite sensitizing effect on the carotid sinus reflex particularly in the presence of coronary disease It is a common practice to administer digitalis preoperatively to elderly patients without congestive failure for the purpose of preventing postoperative circulatory failure Such a practice in our opinion is not rational because the development of congestive failure as a result of surgical procedures is exceedingly rare and when it occurs rapid digitalization usually takes care of the situation Preoperative digitalization on the other hand increases the excitability of the carotid sinus reflex among the functions of which one is to effect powerful cardiac inhibition and cause vasomotor depression As a result of the mechanical procedures often used about the neck during the administration of volatile anesthetics as well as of the increased excitability of the nervous centers during certain stages of the anesthesia excitation of the carotid sinus during surgical operations must occur frequently The combination of such factors may well be responsible for some of the sudden cardiac arrhythmias and the sudden deaths reported as occurring during surgical procedures

Treatment — This depends on the nature of the attacks and on the predisposing causes During attacks loosening the clothing particularly around the neck and placing the patient in a horizontal position result in prompt recovery in the majority of instances If the heart rate is very low or if there is evidence of vasomotor collapse the administration of epinephrin is indicated Depending on the severity of the attack from 0 5 to 1 0 mg (1/120 to 1/60 grain) of epinephrin or from 0 5 to 1 c c (7 to 15 minims) of a 1 1 000 solution may be administered subcutaneously or 0 5 c c (7 minims) of a 1 10 000 solution may be injected slowly intravenously

For the prevention of attacks in patients belonging to the first group with

The spontaneous attacks usually occur when the patient is either standing or sitting They last for from one half minute to three minutes, in rare in tances in cases belonging to the cerebral syncope " group, they are of longer duration The patients usually recover rapidly with no after symptoms other than an occasional headache I have observed but one patient who claimed that for several days following a spontaneous attack she felt weak and exhausted In this patient moderate pressure on the sinus for from three to five seconds resulted in weakness dizziness and but partial syncope nevertheless she claimed that for several days she did not feel well In this instance both the spontaneous and the induced attacks were caused by powerful reflex inhibition of the heart originating from the carotid sinus and it is remarkable that following the attack the arterial pressure which previously had been only moderately elevated became considerably elevated over a period of hours, a type of change not observed in any other subject

Patients with carotid sinus syncope of the third type, "cerebral syncope', often give clinical evidence of unstable vasomotor systems Such symptoms as palpitation hot flushes moist palms and emotional instability frequently are present The heart rate shows fluctuations The arterial pressure tends to fluctuate spontaneously over a considerable range Dermatographia acrocyanosis urticaria and other neurogenic skin lesions may be present The basal metabolic rate may be as low as minus 15 to 20 per cent without clinical evidence of myxedema Often the electric skin resistance is high In an appreciable percentage of cases duodenal ulcer is present Some of these clinical characteristics have been present during the patient s entire life or for many years These clinical earmarks correspond to a bodily state variously designated in the past as vegetative neurosis ' or ' vasomotor instability "

In addition to coronary sclerosis certain other forms of organic disease such as arterial hypertension arteriosclerosis aortic stenosis and syphilis of the central nervous system seem to bear a causative relation to the carotid sinus syncope

Symptoms —The spontaneous attacks often are preceded by aurae such as dizziness weakness epigastric distress and spots before the eyes Some patients have to lie down as soon as these symptoms appear in order to prevent fainting Numbness tingling and coldness of the extremities starting in the fingers or the toes are frequent complaints The majority of the spontaneous attacks are not associated with convulsive movements, but if stimulation of the sinus is prolonged convulsive movements occur A detailed examination of the sequence of events in induced attacks reveals that loss of consciousness usually precedes motor changes in some instances, however, a cataleptic state of the musculature or even mild convulsions precede the onset of mental con

Vago agal Syncope (Adams Stokes Syncope of Reflex Origin)

This term has been applied recently by Weiss and Ferris[1] to cases of syncope of reflex origin in which the entire reflex arc is located within the vagus system The afferent impulses are et up by certain types of stimuli acting on ensory nerve endings of the vagus They travel to the vagus center and thence discharge impulses along the motor fiber of the vagus nerves to the heart which result in lowing of the heart in sinoauricular block in partial or complete block or in total cardiac standstill respectively Hence this type of syncope just as the carotid inus vagal syncope represents a special form of Adams Stokes attack of refl x origin Between attacks the heart and the vascular system may be normal in every respect

Irritation of vagal branches by inflamed tonsils by pathologic changes in the larynx by diverticulum of the esophagus and by carcinomatous growth in the mediastinum or mechanical irritation of the nerves of the bronchial mucosa by the broncho cope are amon the known etiologic factors It is possible that patients who faint on marked d s ention of the stomach and cardia following the swallowing of large amounts of gas belong to this group with reflex syncope Similarly th syncope that instantaneously follows the drinking of cold fluid while in an overheated and fatigued state as after mountain climbing may be vagovagal in origin Some of the drowning acc dents following the ingestion of a heavy meal may well be the result of a gastrovagal inh bition although uch attacks may be vasovagal The hearts of these patients as far as one can as certain are normal in every respect though obviou ly certain types of organic lesions of the conductive system will predispose to the attacks or may make the attacks more serious The carotid sinus reflex and the oculomotor reflex usually are found to be normal when the vagovagal reflex is hyperactive The exception to this rule is a ca e reported by Wei s and Ferris[9] in which there was simultaneous hyperactivity of both the vagovagal and the oculocardiac reflex

In the majority of cases with vagovagal syncope sudden disturbance of the cerebral circulation and the resulting anoxemia are the principal factors in the causation of fainting and unconsciousness but we have indicated that imul taneously activated vasomotor reflexes play a contributory role

The *clinical manifestations* are essentially the same as those of the carotid sinus reflex syncope The patient may have warning in the form of an aura of hort duration or he may collapse without warning The eyes are rolled up all reflexes may be absent and the patient looks as if he were dying Improvement may be as rapid and as unexpected as the onset of syncope or it may not occur for several minutes The frequency of the attacks and their duration vary con iderably depending on the precise etiology There may be but one attack in

cardioinhibitory reflex and irregularities, atropin in doses of 0 5 mg (1/120 grain) twice a day or tincture of belladonna, 1 c c (15 minims) three times a day may be beneficial Ephedrin in amounts of from 15 to 30 mg (1/4 to 1/2 grain) may also be used The latter drug increases the excitability of the myocardium and thereby prevents slowing of the heart rate In the second group of cases with vasodilator reflex administration of epinephrin or ephedrin is indicated during the attack In view of the absence of cardiac inhibition, atropin is not indicated In the third group "cerebral fainting", none of these drugs, in our experience has proved beneficial

If the hyperactivity of the reflex is mainly unilateral, and if the attacks have a tendency to recur at frequent intervals surgical section of the nerve or denervation of the sinus is justified The technique used by Dr Tracy J Putnam and Dr Donald Munro consists in exposing the carotid artery at the level of the bifurcation The internal external and common carotid sheaths are then stripped for a distance of about 2 cm above and below the bifurcation Usually considerable tissue chiefly nerve fibers is found to be strongly adherent to the sinus superiorly just at the fork of the bifurcation This tissue including the sheaths of the internal and external carotid arteries containing the carotid nerve is isolated and sectioned about 8 mm above its junction with the carotid sinus If the operation is performed under general anesthesia or under local anesthesia with attention to the satisfactory infiltration of the nerve tissues only a moderate rise in the blood pressure and a slight increase in the heart rate follows section of the nerve

In only one case observed by Weiss and Baker[17], in which novocainization of the sinus and the nerve structures was not performed was there a marked rise in the arterial pressure following section of the nerve In this 64 year old male patient with attacks of asystole the arterial pressure following section of the right carotid nerve rose from about 140 mm Hg systolic and 90 mm Hg diastolic to 250 mm systolic and 140 mm diastolic The heart rate rose from 40 per minute to 120 The sinus rhythm was altered to auricular fibrillation Within forty eight hours the blood pressure and the cardiac rate and rhythm returned to the preoperative level and rhythm respectively In the experience of Ferris Capps and Weiss[18] denervation of the sinus in selected cases of carotid sinus syncope has proved beneficial The attacks have not returned in 10 to 18 months Bilateral denervation of the sinus has not been undertaken because of the possible damage resulting from the induction of arterial hypertension although it is possible that the depressor aortic nerves can take over some of the functions of the carotid sinus nerves and that eventually the blood pressure may return to its normal level There are animal experiments available in support of such a contention

precipitated usually by the swallowing of food Sometimes only a sip of water caused an attack The syncope was associated with pain along the lower *portion of the sternum descending toward the stomach* The attacks occurred as frequently as two or three times daily in the months preceding admission

Physical examination performed after the patient recovered from the illuminating gas poisoning revealed essentially normal findings with the exception of a heart rate of 48 per minute The electrocardiogram was normal X ray *examination of the esophagus revealed that its lower portion was dilated and that* at the lower third there was a hook shaped diverticulum (Fig 6) Following the discovery of the diverticulum, a small rubber balloon connected with a duodenal tube was swallowed by the patient and was placed at the level of the diverticulum On the distention of this balloon the patient experienced sudden dizziness fol

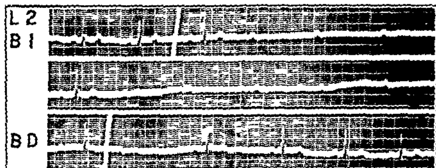


Fig 7 — Electrocardiogram lead II Continuous tracing representing the effect of *inflation (vertical white line of BI) and of deflation* (vertical white line of BD) of the balloon placed at the level of the diverticulum (Fig 6) Inflation induced instantaneous heart block with a long period of ventricular standstill associated with syncope (Courtesy of *Archives of Internal Medicine*)

lowed by syncope Release of pressure promptly relieved the symptoms The manifestations of the spontaneous and induced attacks were identical Electro*cardiograms obtained during such observations* revealed complete auriculoventricular dissociation (Fig 7) Barium chloride failed to prevent or to influence either the spontaneous or the induced attacks Epinephrin and ephedrin in small doses abolished the symptoms although pressure on the diverticulum con*tinued to induce complete heart block* *The observations indicate that these* drugs even in small doses increase the excitability of the ventricles which then make possible the instantaneous development of a regular idioventricular rhythm Atropin abolished both the symptoms and the heart block

Additional observations made in this patient indicated that the changes in

a lifetime, as, for example when a bronchoscopic examination is performed or attacks may recur at intervals of hours for many years

The nature of vagovagal syncope has been studied in detail in a remarkable case observed by Ferris and Weiss The patient was a white male, aged 64



FIG 6 —The appearance of diverticulum of the e ophagus mechanical stimulation of which was followed by complete A-V di ociation of the heart and syncope (Courtesy of Archives of Internal Medicine)

years who entered the hospital in a stuporous state following attempted suicide The cause of this act was despondency because of fainting spells believed to be incurable from which he had suffered for ten years The attacks manife ted themselves in sudden dizziness or fainting, lasting a minute or two and were

A 45 year old male entered the ho pital with blindness in the left eye For one year he had noticed nodes in the right ide of the neck There was also some nasal obstruction The left eye showed proptosis fixed pupil and no movements The fundus showed dilated veins and papilledema and blurring of the di k There were hard nodes in both cervical chains Biopsy on two occasions resulted in a diagnosis of reticulum cell sarcoma The patient developed numerous attacks of dizziness and syncope The spontaneous attacks usually started with pain and sensation of numbness over the left side of the mouth and radiating up into the left eye Simultaneously the heart became slow and irregular The patient be came pale dizzy and if the attack developed in the standing position syncope occurred Pressure over the left eye induced long periods of asystole with sino auricular block accompanied by identical symptoms Pressure over the right eye was ineffective The response to the carotid sinus pressure was also normal Sub cutaneous administration of 1 mg (1/60 grain) of atropin abolished the efficacy of pressure over the left eyeball

Treatment — Administration of atropin in doses of from 0 5 to 1 mg (1/ 0 to 1/60 grain) will abolish cardiac slowing In case of retrobulbar hemorrhage or removable tumors proper urgical procedure will abolish the attacks

Pleural Shock

Ever since the introduction of thoracentesis and of pleural surgery it has been known that irritation of the pleura is at times associated with unpleasant dangerous or even fatal reactions These reactions are at present termed pleural shock by the earlier French Italian and German observers they were described as pleural epilepsy or pleural eclamp ia Thus Forlanini who in 188 advocated the therapeutic use of pneumothorax was familiar with the clinical aspect of the syndrome

Although pleural shock has been investigated carefully both in animals and in man there still exists some lack of agreement as to whether the reactions observed after the introduction of pneumothorax are reflex in origin or whether they result from air emboli That mechanical and chemical irritation of the pleura may induce cardioinhibitory and vasomotor reflexes has been shown by the systematic and excellent studies of Capps and Lewis They have demon strated in dogs a cardioinhibitory reflex with afferent impul es travelling through the pulmonary branches and the pulmonary ganglia to the medullary centers whence motor inhibitory impulses are dis harged to the cardiac vagal endings The vasomotor reflex usually was dilator but at times constrictor in nature The afferent impulses travelled through the posterior root by way of the sympathetic cord to the vasomotor centers whence motor dilator impul es

atropin two or three times daily, or 1 c c (15 minims) of tincture of belladonna two or three times daily, may be effective Ephedrin in amounts of 15 to 30 mg (1/4 to 1/2 grain) two or three times daily, alone or in combination with atropin should be tried if atropin alone fails Unfortunately, however some patients develop rapid tolerance to ephedrin In some cases the attacks are due to inflammation of tissues surrounding the nerves, hence they disappear after subsidence of the infection Surgical excision of the irritating focus is indicated in some cases If this is not feasible, or if the exact location of the focus cannot be determined novocainization of the vagus trunk in the neck should be performed as a diagnostic test first on one side and then on the other If such a test abolishes the attack unilateral section of the vagus trunk may be undertaken in cases of severe type of syncope

Oculovagal Syncope

It has been known since 1908 that moderate pressure over the eyeball induces slowing of the heart without accompanying symptoms in some half of younger normal persons This phenomenon often called the Dagnini Aschner eyeball reflex depends on a vegetative reflex the afferent portion of which is located in the orbital branches of the trigeminal nerves and the motor portion mainly in the cardiac branches of the vagi but in many instances also in the vasomotor nerves The central portion of the reflex involves the trigeminal, vagal and vasomotor centers together with their specific intercommunications Under certain pathologic conditions variations in the motor effects of the reflex may occur

In contrast to the cardiac slowing of carotid sinus reflex origin, the accompanying vasodepressor element of the eyeball reflex is but slight and often is entirely absent A marked degree of cardiac slowing may exist without a fall in the arterial pressure The explanation of this paradox lies in the fact that often simultaneously with the oculocardiac inhibition an oculo vasopressor reflex also is activated Thus the afferent impulses of the trigeminal nerve can activate simultaneously powerful sympathetic as well as parasympathetic reflexes, a fact which constitutes weighty evidence against the value of this reflex as a measure of the so called tonus of the parasympathetic system

The combined presence of the oculocardiac and oculo vasopressor reflexes in the Dagnini Aschner phenomenon explains the relative rarity of syncope of oculocardiac origin as compared with carotid sinus and vagovagal syncope In the presence of irritative lesions of the orbit nevertheless dizziness nausea, vomiting faintness and syncope may occur Severe hemorrhages in and primary or metastatic tumors of, the orbit may be the precipitating factors The following case is cited as an example of syncope of oculocardiac origin

A 45 year-old male entered the hospital with blindness in the left eye For one year he had noticed nodes in the right side of the neck There was also some nasal obstruction The left eye showed proptosis fixed pupil and no movements The fundus showed dilated veins and papilledema and blurring of the disk There were hard nodes in both cervical chains Biopsy on two occasions resulted in a diagnosis of reticulum cell sarcoma The patient developed numerous attacks of dizziness and syncope The spontaneous attacks usually started with pain and sensation of numbness over the left side of the mouth and radiating up into the left eye Simultaneously the heart became slow and irregular The patient became pale dizzy and if the attack developed in the standing position syncope occurred Pressure over the left eye induced long periods of asystole with sino-auricular block accompanied by identical symptom Pressure over the right eye was ineffective The response to the carotid sinus pressure was also normal Subcutaneous administration of 1 mg (1/60 grain) of atropin abolished the efficacy of pressure over the left eyeball

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were transmitted to the splanchnic area Section of the vagus nerves and administration of atropin abolished the cardioinhibitory pleural reflex, but not the vasomotor reflex The effects of the latter could be prevented by the administration of epinephrin

The behavior of the pleuro cardioinhibitory reflex, as observed in dogs, corresponds closely in nature to the first type of cardioinhibitory carotid sinus reflex in man as well as to the vagovagal reflex Indeed, the pleuro cardioinhibitory reflex is but a special form of vagovagal reflex Similar reflexes may originate from irritation of the bronchial surface during bronchoscopy, as we have described previously The vasodilator reflex from the pleura is quite similar in its behavior to the second type (vasomotor) of syncope of carotid sinus reflex origin It is also of interest that in dogs Capps and Lewis have observed that stimulation of the pleura may precipitate the vagal or the vasomotor reflex, either singly or combined In the study of the carotid sinus reflex in man we have also observed that the cardioinhibitory, vasodilator and cerebral types of reflex may occur alone or in various combinations in the same patient

Capps and Lewis have also demonstrated that mechanical irritation of the inflamed pleura can induce more intense and more frequent cardioinhibitory and vasodepressor reflexes than does irritation of the normal pleura and that these reflexes are precipitated through stimulation of the parietal rather than of the visceral pleura They have likewise, demonstrated slowing of the heart and fall in the blood pressure during irritation of the pleura in man They believe that in addition to the degree of inflammation and the intensity of the stimulus other factors such as the amount of fluid removed the rapidity of withdrawal the presence of long standing effusion and senile changes in the heart and blood essels play a role

That some of the reactions seen during the induction of pneumothorax are caused by pleural reflexes rather than by air embolism, is supported by the recent observations of Arnstein and Wischnowitzen [5] These authors measured the heart rate and arterial pressure in o subjects before the introduction of the needle immediately after the skin had been punctured, after the pleura had been punctured and after from 50 to 100 c c of air had been introduced The results indicate that fall in the arterial pressure and slowing of the heart followed puncture of the pleura only they did not follow puncture of the skin or the introduction of air It is also of interest that anesthetization of the pleura or administration of atropin abolished the reflex These observations show that the cardiovascular responses following the introduction of air may be reflex in origin

That air embolism develops when air is introduced in the pleural cavity is probable It has been argued that some of the unilateral manifestations such as tran

sient hemiplegias, or unilateral paresis following the introduction of air into the pleural space must result from air embolus rather than from reflex origin Such a postulation, however, is not necessarily correct for in recent studie with Baker Capps and Ferris it was observed frequently that stimulation of one carotid sinu with proper intensity of the stimulus precipitated subjective sensation, temporary *paralysis or tonic and clonic convulsions only over the opposite side of the body* Thus a reflex of peripheral origin can induce hemisomatic responses That some of the accidents observed following attempted pneumothorax are the re ult of arterial air embolism from entrance of air into pulmonary veins is unquestionable Some authors believe that such accidents are far more common than those due to pleural reflexes

The *clinical manifestations* in pleural shock as in other types of syncope show great variation In the majority of instances there is pallor weakness fainting dizziness and headache examination reveals *a fall in the blood pressure* of from 20 to 40 mm Hg with or without slowing of the heart rate and with weak pulse In the more severe cases the onset is rap d the patient collap es completely unconscious in flaccid paralysis or with mild clonic seizures The re pirations often are shallow rapid and irregular Recovery may be rapid but in older *patients with arteriosclerosis impairment of consciousness* at times with psychosis, may last for from one half hour to several hours Pleural shock may be fatal as judged from the literature such accidents were more common in the past than they have been in recent years

The only fatal pleural shock that I have witnes ed followed my first pleural tap as an interne in Bellevue Hospital New York City The patient a male over 70 years of age exhibited congestive failure of the circulation with anasarca as a result of severe myocardial failure caused by coronary sclero is Puncture of *the left pleura was performed while the patient was sitting on the edge of the bed* Immediately after the needle was introduced into the pleural cavity and fluid appeared the patient cried Doctor I am getting weak you are killing me then he collapsed Instantly the skin became ashy grey with patchy cyanosis no heart sound was audible the previously distended veins collapsed and the pulse was absent Cardiac massage artificial respiration and intracardiac stimulants were of no avail Apparently the patient died instantly The autopsy showed severe coronary sclerosis and myocardial scarring but failed to reveal *anything pertinent to the pleural tap*

Pleural shock may develop not only from puncture or surgical incision of the pleura but also from irrigation of the cavity from movements of drains and at times from pleuritis and external non penetrating blows Severe reactions are frequent in nervous patients particularly those with vasomotor instability in chronically weakened and bedridden patients and in patients with severe heart

disease Some patients requiring pneumothorax develop reactions with each puncture of the pleura, others on one or on few occasions The sitting position for obvious dynamic reasons, predisposes to attacks Hence it is wise to avoid this position whenever possible

Treatment – In the prevention of pleural shock the proper performance of the puncture or surgery of the pleura is most important The patient, particularly if he is of the nervous type should receive sedatives in the form of from 0 1 to 0 2 gm (2 to 3 grains) of sodium luminal or other barbiturates one or two hours before the puncture and about one half hour before he should be given 1 mg (1/60 grain) of atropin subcutaneously Local anesthesia should be applied carefully not only subcutaneously but intrapleurally

Whenever possible the puncture should be performed with the patient lying on his side If he is in the sitting position, he should be well supported The heart rate and the blood pressure should be watched carefully If there is indication of onset of a reaction the needle or the irritating object should be removed and the patient placed in the ecumbent position If the cardiac slowing is marked atropin 1 mg (1/60 grain), injected intravenously or intramuscularly is indicated

If there is evidence of collapse with rapid thready pulse epinephrin in a 1 10 000 solution infused slowly intravenously at a rate of 0 5 c c per minute is useful If the patient is pulseless and there is no evidence of cardiac action massage of the precordial area and artificial respiration with insufflation of oxygen should be undertaken In desperate cases abdominal incision and direct massage of the heart through the diaphragm have been attempted

If the surgical procedures on the pleura are performed under proper precautions and with skill the danger from "shock" is slight

Pericardial Shock

D Agata in 1911 and others have claimed that irritation or trauma to the pericardium may cause a fall in the arterial pressure and cardiac standstill Cocainization of the parietal layer of the pericardium abolishes the responses, indicating that we are dealing with a reflex similar to that in pleural shock The existence of pericardial shock of reflex origin is doubted by most observers Evidence is certainly lacking that in man syncope develops from pericardial reflex irritation

Syncope is observed at times during surgical handling of the pericardium but such attacks develop usually from mechanical obstruction of the blood flow or from suddenly precipitated arrhythmias as a result of irritability of the myocardium

Peritoneal Shock

Reactions following removal of a large amount of fluid from the peritoneal cavity are not rare but it is questionable whether in these instances we are dealing with a reflex similar to that originating from the pleura and the pericardium. In the majority of instances the sudden expansion of the splanchnic vessels is responsible for the syncope.

Syncope from Central Vasomotor Stimulation

Syncope may result from direct stimulation of the vasomotor centers by chemical or mechanical agents. Among the chemical agents acting on the vasomotor centers and leading to collapse the most important are the local anesthetics and other centrally acting drugs such as lobelin and coramin. These drugs through their central action may induce a diffuse dilatation of the minute vessels which then results in a drop in the blood pressure and in partial or complete collapse. The efferent impulses of such a central stimulation are discharged apparently along the efferent vasomotor nerves. Similar responses are observed during surgical manipulations particularly close to or in the hind brain. It is also possible that some of the attacks of syncope occurring rather frequently in patients with brain tumors and following head traumas are due to stimulation of the vasomotor centers.

A special form of syncope which may be termed *syncope of overventilation* also belongs in this group. This type of syncope is due primarily to an *Auspumpung* of carbon dioxid from the blood resulting in a lowered carbon dioxid tension in the medullary centers. Such a change is followed by a fall in the blood pressure and ultimately it may result in apnea and in unconsciousness. The heart rate usually is rapid. It is probable that in the mechanism of this type of syncope in addition to primary changes in the vasomotor centers reflexes from the carotid sinus and from the lungs (Hering Breuer reflex) play a role.

The *clinical manifestations* of fainting spells of vasocentral origin depend on the degree of central vasodilatation. Following the administration of local anesthetics mild reactions are quite common. They manifest themselves in sudden weakness, dizziness and tremor and in pounding of the heart. The face is pale and the skin often is beaded with perspiration. Such mild reactions usually pass in the course of a few minutes. The heart rate is rapid and the pulse small. Both the systolic and the diastolic pressures may exhibit an appreciable fall. In instances with more severe reactions the onset may be rapid. The patient sitting in a dentist's chair may collapse suddenly without warning, the disturbance of the return of blood flow may be so severe that the radial pulse

pend on transient seizures of ventricular fibrillation more often than has been suspected in the past

Schwartz and Jezer[1] have called attention to the fact that this type of syncope may be suspected clinically, if, preceding a period of unconsciousness the heart rate has been noted to increase above the basic rate Such an increase of the basic heart rate is due to premature ventricular beats or to "basic ventricular beats On some occasions aberrant ventricular oscillation may give origin to audible heart sounds or palpable pulse

With the exception of the instances with reflex inhibition discussed under the headings of carotid sinus syncope and vagovagal reflex syncope, cases with Adams Stokes syncope show organic lesions of the conductive system or depression of the conduction induced by structural lesions or by chemical substances The most frequent type of lesion is the presence of arteriosclerotic plaques Rheumatic fever diphtheria syphilis and scarlet fever may be responsible for local disturbances of rhythm Some instances of syncope occurring on effort are of the Adams Stokes type In some patients with organic heart disease the heart rate drops on marked exertion or shows no elevation Thus the relatively or absolutely slow rate is unable to maintain an adequate blood flow

The duration of asystole leading to syncope varies Thus syncope may follow asystole of three seconds in duration, or may be absent even after fifteen seconds Among other factors the condition of the cerebral arteries and the position and activity of the body are important I have observed a 56 year old laborer with complete and permanent A–V block of the heart, who suffered from as many as twenty attacks of syncope with convulsive seizures a day The ventricular rate was usually 38 per minute Whenever it dropped to 1 per minute, the patient would have an attack of unconsciousness and convulsions Following the seizure the heart rate became elevated On one occasion ventricular standstill of sixteen seconds was noted The patient eventually died in one of the attacks

The *clinical manifestations* depend on the degree of slowing of the heart rate as well as on the speed of onset of the cardiac slowing If the asystole is not marked the only symptoms are light headedness, dizziness and sensation of faintness Such sensations frequently are present in patients with various type of heart block If the slowing is sudden and severe, the patient may collapse without warning often injuring himself In such cases there is a generalized pallor and the appearance of collapse Convulsions occur more frequently in this type of syncope than in any other type and often are severe If the slowing comes on gradually and lasts for a prolonged period the patient may be constantly in a semistuporous or at times in a psychotic state I have observed a patient with a heart rate of 28 who felt fairly comfortable while lying flat but

who became temporarily unconscious following the effort of raising the head and upper part of the body

Fatal attacks of Adams Stokes syncope particularly in the presence of permanent heart block are not infrequent In some patients there is a tendency to progressive slowing of the ventricular rate and the attacks increase in frequency until the cerebral ischemia resulting from a long asystole proves incompatible with life

Treatment —In the prevention of attacks measures are used which increase the heart rate and make the ventricular contraction more forceful Atropin, as a rule is not very beneficial In large therapeutic doses such as from 2 to 4 mg (1/30 to 1/15 grains) it may raise the ventricular rate slightly but such doses are associated with undesirable side action In cases in which the syncope depends on vagal depression of the A-V node which has been damaged by organic disease atropin may abolish the complete block or may prevent the transition from sinus rhythm to A-V dissociation Such cases however are rare The administration of barium chloride in doses of from 30 to 60 mg (1/2 to 1 grain) four times a day has been advocated as a preventive measure In my experience in some half dozen cases this medication has not proved useful It is also stated that dried thyroid gland 0 1 gm (1 1/2 grains) of the U S P preparation is effective in the prevention of attacks My observations indicate that it does at times alleviate symptoms in rare instances it may even reestablish sinus rhythm Patients under such treatment should be closely supervised however owing to the possible development of hyperthyroidism Ephedrin on the other hand is often quite effective in the prevention of syncope Ephedrin hydrochlorid in doses of from 20 to 30 mg (1/3 to 1/2 grain) given orally three or four times a day increases the excitability of the myocardium hence in case of a shift of the pacemaker the ventricle instantly takes up a regular idioventricular rhythm In rare instances ephedrin may abolish the block In cases of persistent complete block ephedrin may raise the ventricular rhythm In cases with severe myocardial damage ephedrin is less efficacious

The most effective drug in both the prevention and the treatment of Adams Stokes attack is epinephrin Doses of from 0 2 to 1 0 c c (3 to 15 minims) of a 1 1 000 solution given subcutaneously or intramuscularly every two to four hours invariably increase the heart rate and improve the circulation Sometimes active massage of the site of injection one or two hours after the administration of the drug may result in a secondary though weaker response If prolonged ventricular standstill exists and life is in imminent danger intracardiac administration of 0 5 c c (7 minims) of a 1 1 000 solution followed by cardiac massage is justified

Syncope with Tachycardias

Paroxysmal tachycardias, like sudden bradycardias, often are associated with dizziness and syncope Savini[1] in 1912 spoke of a syncopal form of paroxysmal tachycardia Such a tachycardia may develop in a heart previously normal in rate and function Thus the onset of paroxysmal auricular and ventricular tachycardias and of auricular and ventricular fibrillations is often accompanied by syncope or milder manifestations (Fig 8) Such attacks of syncope, particularly when associated with ventricular tachycardia and fibrillation, may be fatal

It has been shown in animals that a relatively slow heart rate is essential for the optimal filling of the ventricles[3] With an excessively rapid rate the

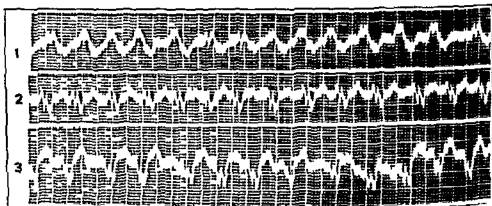


Fig 8 —Attacks of syncope associated with rapid heart rate in a patient 71 years of age During an attack the electrocardiogram reveals a combination of transient ventricular fibrillation and ventricular tachycardia with a few sinus beats

filling and hence the output of the ventricles is below normal The decrease in the coronary blood flow may be out of proportion to the diminished cardiac output Elevation of the cardiac rate above a certain point in man also is associated with a markedly decreased cardiac output, which may cause both precordial pain and cerebral symptoms as a result of myocardial and cerebral ischemia respectively

The changes induced in the circulation of man by a rapid cardiac rate may be illustrated by observations made by us in 1931 on a 17 year old schoolboy who suffered from attacks of paroxysmal auricular tachycardia The onset of these attacks usually was sudden and occurred during exertion The patient experienced sudden faintness dizziness and nausea followed by moderate orthopnea and dyspnea The hemodynamics of the circulation were compared during

and after an attack In one attack while the heart rate as indicated by the electrocardiogram was 10 to 230 the output of the heart as determined by the dye method was 2 4 liters and the stroke volume between 10 and 11 c c The oxygen difference of the femoral arterial and venous blood was 13 7 volumes per cent The vital capacity of the lungs was 500 cm The arterial pressure was 88/78 mm Hg and the venous pressure 13 cm H O The day following the attack the heart rate with a sinus rhythm was 78 per minute the cardiac output 5 8 liters per minute the stroke volume 74 c c the oxygen difference in the leg 3 1 volumes per cent the vital capacity 3 00 c c the arterial pressure 110/65 mm Hg and the venous pressure 11 cm H O In this case the insufficiency and derangement of the circulation caused by the rapid heart is clear In addition to the decreased cardiac output and the cerebral ischemia the onset of an abnormal rhythm may be responsible for precordial distress and may set up certain cardiac reflexes which are important in the precipitation of attacks Thus syncope may be associated with simple coupled premature beats without any appreciable fall in the arterial pressure

Barnes[13] found 15 cases with cerebral symptoms in a group of 104 cases *exhibiting paroxysmal tachycardia Vertigo was present in 8 temporary blind* ness in 6 syncopal attacks in 4 and epileptiform seizures in 2 The same patient exhibited various symptoms in the same or in different paroxysms The prognosis was not affected by the presence or absence of the attacks In some patients the paroxysm of abnormal rhythm is precipitated by effort hence an apparent relationship existed between exertion and the appearance of syncope

Treatment — The treatment of this type of syncope consists in treatment of the cardiac irregularity

Syncope Anginosa

Some patients suffering from angina pectoris develop syncope with some or with all of the anginal attacks Nothnagel has described syncope associated with angina like pain under the syndrome angina pectoris vasomotoria It is questionable however whether these patients suffered from true angina The clinical aspects of attacks of syncope and of true angina pectoris recently have been described by Gallavardin but the exact nature of the attacks is not yet clearly understood

It has already been stated that in some subjects any type of intense pain may precipitate syncope therefore one possibility is that the syncope depends solely on the intensity of pain Clinical analysis suggests however that pain of cardiac or of abdominal origin is more apt to precipitate syncope than pain of other origin Thus it cannot at present be stated definitely whether the in

tensity of cardiac pain, the specific cardiac reflexes set up by the coronary spasm or finally an acute myocardial weakness caused by ischemia from the spasm of the coronary arteries, alone or combined, are responsible In some instances the syncope is associated with non painful or slightly painful angina, suggesting that pain alone is not always a factor I have observed a 66 year old patient who suffered from arterial hypertension coronary sclerosis and cardiac asthma and in whom the attacks of syncope were associated with but slight precordial distress The precipitating causes of fainting were exertion, emotional excitement and overeating the same factors usually responsible for angina and paroxysmal dyspnea

While cases of true syncope caused by angina are relatively rare, dizziness, weakness instability on standing and a sensation of marked faintness, often associated with pronounced angor animi, are frequent manifestations during anginal attacks In some cases of angina syncope appears only with the onset of severe attacks and offers a rather grave prognosis Death sometimes occurs during syncope

The cardiac rhythm and rate during the syncope vary, in only rare instances is there marked slowing of the heart Gallavardin[41] has described a patient suffering from angina pectoris who developed syncope and heart block with some of the attacks In rare instances ventricular fibrillation of short duration may appear with the syncope, but this type of arrhythmia occurs less frequently than has been claimed in the past In other instances there is no change in the cardiac rate or rhythm but measurements of the blood pressure and observation of the pulse indicate that the contractile force of the heart is less than under normal conditions Such impairment of the contractile force of the heart in the presence of angina probably is the most common cause of syncope, in view of the fact that intense vasoconstriction of the coronary vessels occurs during attacks Hence in anginal attacks weakness of the myocardium predisposes to cerebral ischemia

Syncope may also develop as a result of *coronary thrombosis* The underlying mechanism in such cases is essentially the same as the circulatory changes accompanying angina pectoris In rare instances syncope may be the only clinical manifestation of coronary thrombosis Pain prostration and subsequent pericardial friction rub fever and leukocytosis may be absent and only the appearance, days later of definite and progressive alterations in the complexes of the electrocardiogram indicates coronary thrombosis as the underlying cause of syncope

Treatment —The management of syncope anginosa should consist in the application of measures to relieve the angina pectoris method described elsewhere in Oxford Medicine

Syncope Related to Congestive Failure of the Circulation

Among patients with failing circulation syncope particularly upon effort, is not a rare occurrence in certain types of heart disease it is quite frequent Thus patients with the narrow fishmouth type of mitral valve with advanced *aortic stenosis and with congenital heart disease particularly if it is associated with* congenital diffuse narrowing of the aorta are apt to exhibit syncope when suddenly exerting themselves as in lifting a weight or in running after a street car Similarly young patients with free aortic regurgitation and congestive failure may develop syncope on severe exertion Patients with arterial hyper tension and myocardial failure not infrequently faint in this group fainting may occur without evidence of congestive failure (vascular crisis encephal opathy) Similarly patients in severe attacks of cardiac asthma (paroxysmal dyspnea) sometimes lose consciousness suddenly Acute pulmonary edema regardless of its etiology is associated frequently with fainting and a state of unconsciousness

In all these instances of syncope the most important causative factor is the relationship existing between the condition of the cerebral vessel and the demand of the tis ues for oxygen on the one hand and the cardiac output on the other hand In mitral stenosis and in congenital heart disease with myocardial failure the cardiac output is particularly low and sudden exertion increases the oxygen debt of the tissues including the brain Under these conditions there is a tendency to collapse of the circulation and to severe cerebral anoxemia There may also be a derangement of the circulation in the pulmonary circuit A similar condition exists in the presence of severe cardiac asthma with a tendency to pulmonary edema In patients with arterial hypertension on the other hand the spastic state of the peripheral arteriolar system represents increased per ipheral resistance and an added burden to the heart Hence cerebral ischemia may develop without loss of myocardial strength

The *clinical manifestations* of syncope occurring in patients with myocardial and valvular heart disease depend mainly on the severity and duration of im balance between the circulation and the activities of the ti sues Unconscious ness may be of but a few seconds duration or it may last for several minutes as in the presence of pulmonary edema Its onset may be either sudden or gradual Often because of stagnation of blood in the depots of the cutaneous ves els the patient may be cyanotic, and the veins may be full The heart rate usually is rapid The blood pressure may be low normal or elevated Pul monary signs of congestion or of edema frequently are present Involuntary micturition or defecation may occur The return of consciousness may be abrupt or gradual

Treatment.—The management of syncope associated with acute congestive failure consists in the treatment of the latter condition. As this type of syncope frequently is associated with acute congestive failure and pulmonary edema, the treatment often requires intravenous digitalization.

Syncope of Postural Hypotension

Patients with severe postural hypotension may exhibit fainting, particularly following an abrupt change from the horizontal to the upright position. The clinical symptoms depend mainly on alterations in the arterial pressure resulting from postural changes. While the arterial blood pressure usually is normal or elevated when the body is in the horizontal position, in the upright position both the systolic and the diastolic pressures become considerably lowered in this type of individual. In normal subjects, on the other hand, the systolic blood pressure shows but a slight drop, and the diastolic pressure is slightly elevated. Moreover, contrary to the behavior in normal persons, the heart rate frequently does not become elevated even on prolonged standing. Thus the fundamental defect seems to be in the inability of the blood pressure regulatory mechanisms to adapt themselves to postural changes. From the data available it is impossible to state at present whether the immediate cause of syncope is cerebral anoxemia, sudden loss of intracerebral pressure resulting from cardiovascular changes, or reflex action of these changes on certain centers. Although Gowers[1] has suggested that decreased intracranial pressure may be an important cause of syncope in general, it is questionable whether such change ever is responsible for fainting. Thus personal experience and questioning of others having extensive experience with spinal and cistern punctures indicate that reduction of the spinal fluid pressure is not associated with syncope. It is an interesting fact that one observes syncope less frequently following spinal taps than following simple venepunctures.

Postural hypotension in mild form is present frequently in patients suffering from tabes dorsalis and from other types of spinal cord lesions in which the sympathetic centers and tracts are involved.

Patients with postural hypotension frequently complain of dizziness, headaches and a sensation of faintness on prolonged standing, but cases with syncope on sudden standing up are comparatively rare. Such cases have been reported by Ghrist and Brown[41]. Often these patients show absence of sweating and suffer discomfort in hot weather. At night they may pass large quantities of urine as compared with the amount voided during the day. The behavior of these patients with syncope dependent on postural hypotension is not unlike that of patients with Adams-Stokes attacks or vasovagal syncope except for

the fact that they do not exhibit an absolute cardiac inhibition although a lack of elevation of the heart rate in the upright position is characteristic in typical cases

A case of this type of syncope was observed recently by Dr L B Ellis and myself The patient, a woman 68 years of age suffered from severe attacks of weakness dizziness and faintness particularly when changing her posture from horizontal to upright She had mild diabetes Exudates were present in the retina There was a systolic murmur over the precordium particularly over the pulmonic area Varicose veins were present over the legs and there was *diminished acuity of the sensations of touch pain and heat over the* lower portions Electrocardiograms showed evidence of left ventricular pre ponderance otherwise the laboratory studies revealed nothing pertinent The blood pressure showed such variations as 144/86 to 84/58 142/76 to 76/60 or 152/84 to 65/55 on changing from the horizontal to the standing position on *different occasions These variations were associated with dizziness and faint* ne s and at times the patient was forced to lie down in order to avoid fainting It is of interest that in this case as in other cases reported in the literature no change or only a slight change occurred in the heart rate in spite of marked changes in the blood pressure

Syncope somewhat similar in nature to that observed in patients with postural hypotension occurs in normal persons who suddenly awakened in fright by the ringing of a bell or by some other noise jump up practically before they are awake Under such conditions they may experience a sudden sensation of faint ness or actual syncope

Postural hypotension associated with syncope is common among patient suffering from intense pain or from chronic disability This fact was known to physicians of the remote past, and they took therapeutic advantage of it Thus it is said[12] that before the introduction of volatile anesthetics it was the usual custom in Baron Larey s Hopital in Paris to lay the patient on his back and then to raise him suddenly to the standing posture whenever they wished to induce fainting for the purpo e of relaxing muscles in cases of dislocation

Whether the *syncope experienced by aviators* particularly during sudden looping depends on changes in posture and gravity resulting in marked hypotension is not definitely known The appearance of the subject suggest cranial ischemia The fact that some flyers state that the tendency to syncop can be overcome by sudden straining or shouting suggests that increased intr abdominal pressure may at least partially counteract the circulatory changes This would indicate that sudden accumulation of blood in the abdominal va cular depots is an important factor in this type of syncope Whether in addition to the postural and gravity factors vasomotor refl x s s ch a the carotid sinus

reflex, play a contributory role cannot be stated at present There is also a possibility that, depending on the type of looping, cerebral ischemia and hyperemia may alternate

Syncope is common among ambulatory patients with Addison's disease (adrenal insufficiency) These attacks are caused by hypotension, which is accentuated by the upright posture Hemorrhage into the adrenal glands (adrenal apoplexy) may be associated also with fainting

Treatment — In the treatment of syncope of postural hypotension abdominal supports and corsets may be useful In severe instances the only drug of distinct benefit is ephedrin It should be given in doses of 15 to 30 mg (¼ to ½ grain) three or four times daily The use of ergotamin in doses of 0 5 mg (1/120 grain) twice or three times a day has been advocated, but it is of doubtful value

Syncope Due to Cerebral Engorgement

The exact nature of this type of syncope is not clear, it may be but a special form of syncope of central vasomotor stimulation Gowers[1] (see p 15 of this reference) has pointed out the fact that stooping or lowering the head sometimes causes momentary loss of consciousness He believed that under such conditions there was an increase in the amount of blood in the vessels and that the sudden rise in the intracranial pressure produced the syncope Flexion of the neck also may hinder the return of venous blood flow Gowers discussed the behavior of a woman aged 38 years, who suffered from epileptic attacks in the night as well as during the day The seizures began with a sensation of sudden rush of blood to the head followed by loss of sight and subsequently loss of consciousness It is of interest that stooping induced attacks in which there was a sensation of sudden rush of blood to the head and complete loss of sight but no actual loss of consciousness These manifestations gradually disappeared when the patient stood up

Through the courtesy of Dr Paul D White and Dr William Lennox I have had an opportunity to see a patient with attacks of somewhat similar but more striking nature This patient[43] was a robust stolid Irish coal worker 24 years of age who for over two years had been incapacitated by a severe congestion of the vessels of the head and neck whenever he was moderately active, or lay with his head low or stooped over If he continued to stay in a recumbent position, or if he performed vigorous physical exercise for several minutes he became distressed and sometimes lost consciousness A vigorous attack of vomiting ended the syncopal attack, and immediately he was all right provided he resumed the upright position He has fainted on occasions when cleaning the

wheels of his motor car or when chopping wood Washing his face gave him a choking feeling in his throat and a buzzing sensation in his ears He had to sleep *in an inclined position According to a recent follow up report* the attacks still continue to recur

This crippling condition started several years ago after the subject had been trapped in a bin by loose coal which compressed him up to his waist He had to struggle in order to free himself On the day after his return to work which was a little more than two weeks after his accident his fellow workmen noticed the cyanosis of his face

On physical examination the only abnormal finding was the occurrence of vascular congestion under the above conditions On such occasions a flush appeared over the face and neck with a V shaped line of demarcation up to the base of the neck The congestion was most marked in the forehead and ears *With the progress of congestion cyanosis gradually developed particularly over* the face and ears On standing the hands when hanging were quite cyanotic moist and clammy The heart lungs abdomen and extremities were normal except that the heart rate tended to be accelerated and the venous pressure in the arms was somewhat increased There were no symptoms or signs of obstruction of the superior vena cava The arterial pressure was 135 mm Hg systolic and 80 mm diastolic Neurologic examination revealed normal findings

Injections of epinephrin pituitrin and histamin made his condition wor e

Recently we have had an opportunity to observe a somewhat similar case in the Boston City Hospital The attacks of dizziness and weakness in this young male adult started following an injury to his back On stooping his face became intensely engorged while on standing his hands and feet were red and cyanotic and there was a burning sensation particularly over the feet In this and in the preceding case there was a loss of tonus of the minute vessels of the face hands and feet and presumably also of the brain

Another type of cardiovascular mechanism leading to cerebral hyperemia and syncope is illustrated by the remarkable behavior of a 23 year-old shoe worker whom I have described recently[44] The patient s chief comp aints were dizziness and throbbing headaches of four weeks duration On the day of admission he collapsed He had had a similar attack following a throbbing head ache three years before The past history was uneventful except that he was a rather high strung person and had had much anxiety lately The physical examination following admi sion revealed a heart rate of only 48 per minute The size of the heart was normal and the sound regular No murmurs were elicited The electrocardiogram was normal The systolic blood pressure was 120 mm Hg but the diastolic was 20 mm The venous pressure was normal 1 cm H O There was distinct capillary pulsation and a loud pistol shot

vascular changes induce the cerebral manifestations Among the presenting symptoms of patients with arterial hypertension headaches dizziness nervousness and weakness are common[4] At times such patients complain of a sudden sinking feeling and claim that they are forced to sit down in order to prevent syncope These manifestations have been attributed by us to instability of the vasomotor system rather than to a definite spastic state of the cerebral arteries Whether the more severe cerebral manifestations such as complete unconsciousness convulsions and transient palsies are the result of local spasm has not been determined The elevated spinal fluid pressure the presence of cerebral edema and the normal oxygen difference between the blood of the carotid artery and that of the internal jugular vein all speak against the existence of extensive vascular constriction[46] The evidence available might be interpreted in favor of local or general vascular relaxation rather than of constriction of the cerebral vessel

Some of the cerebral manifestations of uremia with arterial hypertension probably are related closely in nature to the vascular crises and encephalopathy of arterial hypertension Whether all these manifestations of patients with arterial hypertension should be considered as a type of syncope or as a special form of epileptic seizure is debatable Vascular accidents not infrequently are preceded by or associated with syncope

Treatment —In cases with neurosis the syncope disappears with regained emotional equilibrium In rare instances with relaxed vascular system treatment is unsatisfactory and such patients should avoid stooping In syncope with arterial hypertension rest administration of sedatives and at times venesection are beneficial

Syncope Caused by Pulmonary Engorgement

Sudden changes in the pressure relations in the pulmonary circuit may lead to syncope Both increase and decrease in the volume of the vascular bed and in the intrapulmonary pressure may be responsible for such attacks of fainting Thus syncope may be the result of voluntary or of involuntary increase in the pulmonary pressure with the glottis closed Such a Valsalva experiment may induce fainting not only in voluntary subjects but also spontaneously in patients with neurosis The examination of the mechanism of such fainting in neurosis reveals that the patient involuntarily closes his glottis and induces an increased pressure within the alveoli which in turn partially or completely compresses the pulmonary capillary vessels and obstructs the venous flow from the periphery This results in a decreased filling of the ventricles and a sudden diminution of the cardiac output as indicated by the small pulse and the fall in the arterial pressure The size

over both femoral arteries The Kahn test of the blood was negative The white blood cells and the urine were normal

When the patient was approached for a venepuncture, soon after his arrival at the hospital, he became alarmed, complained of dizziness and fainted During unconsciousness the face and skin in general were flushed The capillary pulsation became intense The systolic arterial blood pressure was 150 mm Hg and the diastolic o mm The heart rate was 62 per minute In order to check this observation two hours later repeated measurements of the heart rate and the arterial blood pressure were made, and the patient was again approached with a hypodermic syringe and needle Immediately the systolic blood pressure rose from an average of 130 mm Hg to 185 mm, and the diastolic pressure fell from o mm to o The heart rate rose from 56 to 63 per minute The palpable arteries showed marked pulsation, the capillary pulsation now became intense and the face flushed The patient complained of headaches dizziness and faintness This observation was repeated twice with the same result

During his stay in the hospital the patient was reassured and his anxiety subsided The systolic blood pressure dropped to 120 mm Hg and the diastolic became stabilized at 50 mm The pistol shot and the capillary pulsation no longer could be elicited The sight of the syringe and venepuncture caused no change in the systolic or diastolic pressure

Thus in this patient an emotional storm induced relaxation of the arterioles, resulting in peripheral signs These alterations in the vascular system became intensified during added anxiety With improvement of the mental state the vascular changes and signs as well as the attacks of syncope disappeared I have observed other instances of neurosis with relaxation of the minute peripheral vessels resulting in a low diastolic pressure with normal systolic pressure and in peripheral signs usually accompanying aortic insufficiency These patients often complain of lightheadedness, headache and weakness

Patients with *polycythemia* often experience attacks of severe dizziness and a sensation of faintness Syncope is also a relatively frequent symptom The engorged state of the cerebral vascular system may well be the responsible factor

The syncope that follows lowering of the head and bending of the neck in patients with obstruction of the superior vena cava, as for example when tying shoe laces belongs to this type of syncope Whether the syncope experienced by aviators while "looping" is caused by cerebral engorgement or by cerebral ischemia with splanchnic dilatation is not known

Syncope and its variants occur quite frequently in patients with arterial hypertension The exact mechanism of this type of transient episode is not known but it is often assumed that localized or generalized cerebral vascular spasms (vascular crises) are responsible It is doubtful, however, whether the same type of

arterial system rather than by a disturbance of the heart Obviously no proper method were available to Nothnagel for the analysis of the underlying mechanisms Therefore it is difficult to state whether the cases fall in the group of syncope anginosa or in some other group Precordial pain numbness palpitation and the other findings observed by Nothnagel have been present in some of the subjects observed by us with typical vasovagal carotid sinus and vagovagal syncope In the light of present knowledge the Nothnagel syndrome cannot be considered as an entity deserving separate classification

Gowers Syndrome

Sir William Gowers in 1907 called attention to a group of patients with varied and mostly sensory and subjective symptoms These patients were chiefly women and he has attributed the disturbances manifested during attacks to functional changes in the vasomotor system and the vagus nerves The attacks usually come on gradually with a sensation referred to the epigastrium described as a sense of oppression or of fullness This sensation may ascend to the chest There is seldom nausea and never vomiting A sensation of respiratory distress with difficulty in breathing is common A feeling of orthopnea may also occur as well as acute pain over the heart with a sensation of sudden stoppage followed by rapid action There is sometimes a sense of intense fear and dread without detectable cause Although there is no impairment of consciousness in typical cases, the mental processes are slow and difficult Sudden physical fatigue may be present The face is pale the extremities are cold and the pulse usually is small Shivering is common Tingling and numbness of the limbs particularly over the extremities may be present at times with tetanoid spasm According to Gowers the attacks as a rule have no relation to epilepsy although in some cases they bear a similarity to epileptic seizures He suggests that these vagal attacks may belong to the borderland of epilepsy The attacks are never very brief they usually last over ten minutes and may continue for half an hour or more

Gowers made no study of the cardiovascular system between or during attacks in the cases which he reported nor did he attempt to elicit the underlying mechanisms In this respect his study is less complete than that of Nothnagel although the symptomatology in some of the cases bears striking resemblance to that described by Nothnagel Gowers clearly recognized the distinction between his cases and cases with simple cardiac faints Although Gowers has used the terms vagal and vasovagal attacks to describe these seizures little evidence can be found in his writings as has been pointed out also by Lewis[3] that the attacks bear any relation to disturbances of the vagus or of the vasomotor

of the heart becomes markedly decreased, and its shape is like that of the cor pendulosum Whether in addition to these mechanical factors, pulmonary reflexes are active in this type of syncope we do not know

A similar type of syncope with a somewhat different disturbance of the circulation may be induced by prolonged compression of the thora followed by sudden release Such compression of the thoracic cage not only results in giddiness weakness and faintness but at times causes fainting even in normal persons On such occasions the previously compressed pulmonary vascular bed suddenly dilates both actively and passively resulting in a temporary stagnation of blood in the lungs and a sudden temporary decrease in the peripheral blood flow The metabolites retained in the lungs and the pulmonary engorgement may activate pulmonary reflexes but so far as I know this aspect of the problem has never been studied

Treatment — This consists in prevention or avoidance of increase in pulmonary pressure with a closed glottis or of mechanical compression of the thorax

Syncope with Dissecting Aneurysm

Syncope may be the first manifestation of dissecting aneurysm It may occur without thoracic pain The attacks usually are of short duration No exact observations have been made on patients during this type of syncope In view of the fact that the origin of the dissection is near the branches of the aortic depressor nerves, it may be that we are dealing with a reflex syncope somewhat analogous to the carotid sinus syncope[4]

Nothnagel s Syndrome

Related to syncope anginosa is the so called syndrome of "angina pectoris vasomotoria Nothnagel in 1867 described the behavior of four patients without apparent heart disease who developed attacks of severe palpitation associated with a sense of anxiety, dizziness and syncope The attacks usually start with a sensation of coldness numbness and tingling over the hands and feet These sensations may involve the entire extremities and at times the trunk as well There may be a slight sensation of dyspnea The skin is pale There is pain over the precordium, at times associated with a feeling of anxiety and fear of impending danger such as occurs in angina The radial pulse is small Often there is profuse perspiration The sensation of the skin over the extremities is diminished The heart rate is unaltered or moderately diminished Consciousness is disturbed but not lost The attacks last for from fifteen minutes to an hour

Nothnagel claimed that the attacks were caused by a generalized spasm of the

arterial system rather than by a disturbance of the heart Obviously no proper method were available to Nothnagel for the analysis of the underlying mechanisms Therefore it is difficult to state whether the cases fall in the group of syncope anginosa or in some other group I recorded pain numbness palpitation and the other findings observed by Nothnagel have been present in some of the subjects observed by us with typical vasovagal carotid sinus and vagovagal syncope In the light of present knowledge the Nothnagel syndrome cannot be considered as an entity deserving separate classification

Gowers Syndrome

Sir William Gowers[4] in 1907 called attention to a group of patients with varied and mostly sensory and subjective symptoms These patients were chiefly women and he has attributed the disturbances manifested during attacks to functional changes in the vasomotor system and the vagus nerves The attacks usually come on gradually with a sensation referred to the epigastrium described as a sense of oppression or of fullness This sensation may ascend to the chest There is seldom nausea and never vomiting A sensation of respiratory distress with difficulty in breathing is common A feeling of orthopnea may also occur as well as acute pain over the heart with a sensation of sudden stoppage followed by rapid action There is sometimes a sense of intense fear and dread without detectable cause Although there is no impairment of consciousness in typical cases, the mental processes are slow and difficult Sudden physical fatigue may be present The face is pale the extremities are cold and the pulse usually is small Shivering is common Tingling and numbness of the skin particularly over the extremities may be present at times with tetanoid spasm According to Gowers the attacks as a rule have no relation to epilepsy although in some cases they bear a similarity to epileptic seizures He suggests that these vagal attacks may belong to the borderland of epilepsy The attacks are never very brief they usually last over ten minutes and may continue for half an hour or more

Gowers made no study of the cardiovascular system between or during attacks in the cases which he reported nor did he attempt to elicit the underlying mechanisms In this respect his study is less complete than that of Nothnagel although the symptomatology in some of the cases bears striking resemblance to that described by Nothnagel Gowers clearly recognized the distinction between his cases and cases with simple cardiac faints Although Gowers has used the terms vagal and vasovagal attacks to describe these seizures little evidence can be found in his writings as has been pointed out also by Lewis[3] that the attacks bear any relation to disturbances of the vagus or of the vasomotor

system. The term vasovagal syncope used recently by Lewis defines an entirely different syndrome from that described by Gowers.

In the light of the existing knowledge of the underlying mechanisms of syncope and epileptic seizures, it is difficult to determine the exact nature of the syndrome presented by the patients studied by Gowers. The condition probably does not present an entity in the light of present knowledge. Some of the cases may fall in the group described as 'cerebral type' of carotid sinus syncope (carotid sinus syncope type 3), some may fall in the group of vegetative neurosis, and some may have suffered from milder attacks of epilepsy. Several later writers have reported as Gowers' syndrome attacks entirely different in nature from those presented by Gowers.

The Differential Diagnosis of Syncope

Syncope and Epileptic Seizures

It has been shown earlier in this chapter that syncope is not induced by a single type of mechanism but that a number of functional and organic disorders are responsible for its occurrence. Vasomotor changes depending on posture, widespread autonomic reflexes, chemical substances affecting the walls of minute vessels, and functional and structural changes within the heart are some of the more significant factors leading to fainting and associated manifestations. It has also been pointed out that, while sudden changes in the arterial pressure and in the blood flow play an important role in the precipitation of the attacks, cerebral anoxemia cannot be held as the sole stimulus responsible for syncope.

The degree of cerebral anoxemia, as judged from the study of the cardiovascular systems of patients in the state of syncope, varies considerably even in subjects with the same type of syncope. A study of certain reflex syncopes, particularly those of carotid sinus origin, revealed that in some types of syncope diffuse cerebral anoxemia which could adequately explain fainting and other bodily changes did not exist. Thus Ferris, Capps and Weiss[18] recently presented evidence leading to the conclusion that a special area or areas exist in the brain for the regulation of the conscious state. In their opinion the center or centers are sensitive (*a*) to certain types of sudden change in the systemic and cerebral circulation and (*b*) to reflex influences which may act on the nerve structures of the centers directly or indirectly through localized vascular changes. There also exists some experimental and clinical evidence in support of the contention that fainting and unconsciousness in general depend on the special function of the cerebral center. Pavlov[49], using his technique of conditioned reflexes, found that peripheral reflexes, through their irradiating effect on the cortex, induced a

leep-like condition in animal It has also been shown by Spiegel and Inaba[19] by Hess [0] and by Ranson [1] that certain types of lesion of the midbrain particularly in and around the hypothalamu induce a long deep sleep-like state Similarly lesions of this area caused by tumors or encephalitis may result in a sleep-like unconscious state

The concept that a primary irritability of the center of consciousness in addition to the circulatory element is an important factor in the development of fainting explains the apparent difference in frequency of attacks accompanying the same type and degree of circulatory change It is well known also that some persons faint more easily than others These person in our opinion have a more sensitive center of con ciou ness in the midbrain Such a behavior of this center is entirely analogous with the pronounced variations in the sensitivity of other known and better studied midbrain and hindbrain centers Ju t as the individual convul ive tendency in the presence of a certain type of cerebral lesion is a determining factor in the development of epileptic seizure so the fainting tendency on the one hand and the circulatory and reflex factors on the other determine the occurrence of fainting

The fact that peripheral reflexes can induce syncope without appreciable changes in the systemic circulation and without general cerebral anoxemia is particularly significant because it indicates that syncope may be entirely neurogenic This finding then brings the pathogenesis of certain types of syncope close to that of epileptic seizures and suggests that in some in tances eparation of the two conditions may be difficult Clinical experience i in entire harmony with such a theoretical contention notwithstanding the fact that it is often stated that a number of features definitely differentiate faints from fits

It is generally believed that syncope depends primarily on changes in the cardiovascular system It is often stated that no aura precedes its onset The attacks develop in the ortho tatic position and are not associated with convul ions or other motor manifestations They are usually of hort duration with prompt recovery of con ciou ness and are not apt to recur Fits or eizures on the other hand are said to depend on primary changes in the brain It is claimed that the attacks are preceded by an aura They may occur in any position of the body They manifest themselves in convulsions and oth r motor disturbances Following the eizures there is a period of confu ion and the attacks are apt to recur with greater intensity

For practical purposes these differential features have decided merit and in certain types of yncope or seizure they hold true But just as the examination of the pathogenesi of syncope and of epileptic seizures reveal no sharp demarcation between the two condition so the study of the clinical aspects reveals no rigid differences Practical experience in clinical medicine bears evidence that the

classification of certain transient attacks of unconsciousness often involves great and not infrequently insurmountable difficulty Thus, the study of a large number of cases with syncope revealed that cardiac, carotid sinus and other types of syncope may be preceded by aurae Fainting may also be associated with convulsions micturition defecation and other vegetative functions Recovery, though usually prompt may be followed by a state of confusion Attacks of syncope like epileptic fits may recur at varying intervals for a period of years Adams Stokes type of syncope may develop in the horizontal position Epileptic seizures on the other hand, may have many of the characteristics attributed to syncope *Petit mal* attacks which represent the common type of epileptic seizure may be unassociated with convulsions Vasomotor changes frequently accompany such attacks as is the case in certain types of syncope Emotions may play a primary precipitating rule in ' fits , as they do in fainting

Thus many of the differential characteristics of the two types of attacks are relative rather than absolute Gowers has stated that at times repeated syncope seems to pass into minor epilepsy and he has claimed that " such cases constitute evidence that the state of nerve elements i the same in the two conditions, " He grouped faints vagal attacks , vertigo migraine and " sleep symptoms " under the heading of the borderland of epilepsy Recent investigations conducted in our laboratory not only support such a clinical contention, but they have brought to light changes underlying certain types of syncope which now offer a rational basis for the clinical evidence

In the differential diagnosis of syncope and epileptic seizures therefore as in many other differential diagnostic problems the sum of the evidence, rather than a single qualitative difference is the deciding factor

Some of the predisposing factors and clinical characteristics of syncopal and epileptic attacks are compared in accompanying Table I The comparison

TABLE I

Comparative Features of Syncope and of Epileptic Seizures

Predisposing Factors	*In Syncope*	*In Epilepsy*
Emotion	Frequent	Fairly frequent
Physical fatigue	Frequent	Fairly frequent
Irritating lesions of viscera	Frequent	Rare
Vascular reflex	Frequent	Rare
Cardiovascular disturbance	Frequent	Rare
Inherited constitution	Probably rare	Probably rare
Upright position	Frequent	Frequent
Horizontal position	Rare	Frequent
Sleep	Rare	Frequent
Age	Any	Any

Manifestations of Attacks	*In Syncope*	*In Epilepsy*
Aura (visual auditory sensory)	Frequent	Frequent
Duration of aura	Very short	Relatively prolonged
Anxiety or anima	Frequent	Frequent
Olfactory aura	Rare	Frequent
Sudden onset	Relatively frequent	Frequent
Loss of response with maintained motor function	Rare	In petit mal common
Color of face	Pale	At first pale then flushed
Convulsions	If present mild preceded by collapse	Often initial and severe
Biting of tongue	Rare	Common
Perspiration	Frequent — cold	Frequent — warm
Heart rate	Slow normal rapid	Normal or rapid
Blood pressure	Usually low at time normal	Normal or elevated
Weak or absent pulse	Common	Rare
Respiration	Quiet shallow or slow	Stertorous and labored
Vomiting	Frequent	Frequent
Micturition	Fairly frequent	Frequent
Defecation	Rare	Frequent
Duration of attacks	Short (seconds or minutes)	Longer
Post seizure confusion	Rare	Frequent
Post seizure headache	Frequent — mild	Frequent — severe
Amnesia after attack	Frequent	Frequent

indicates that each feature of syncope can be present also in epileptic fits and vice versa The essential differences are quantitative rather than qualitative The following are some of the differences which are helpful in the clinical diagnosis If careful clinical investigation of the case fails to reveal the etiology this favors an epileptic seizure In the majority of instances the pathogenesis of syncope in contrast to epilepsy is clear and the attacks often occur under somewhat similar conditions Attacks occurring in sleep are strongly in favor of epilepsy again with the exception of Adams Stokes attacks caused by a sudden drop in the heart rate or by paroxysmal arrhythmias which may develop in sleep Aurae may occur in syncope but usually they are of short duration olfactory aura in fainting is particularly rare Convulsions if present in syncope usually are mild Here again there are rare exceptions as prolonged asystole may be associated with the explosive type of convulsions In syncope however convulsions practically

always are preceded by pallor and early manifestations of fainting, whereas in epilepsy the attack may start with convulsions while the patient is still standing Thus it is rare in syncope for motor function to be maintained while unconsciousness is present as may be the case in certain types of so called *sensory epilepsy* or in attacks of *petit mal* In syncope the face is pale and cold, in epilepsy after an initial transitory pallor it is flushed and warm The skin is covered with cold perspiration in syncope and with warm sweat in epileptic attacks Biting of the tongue is rare in syncope it is common in epilepsy The heart rate in syncope often is slow in epilepsy it is normal or elevated The blood pressure, while usually low in syncope is normal or high in epilepsy In contradistinction to epileptic seizures recovery from syncope is prompt and post seizure symptoms are mild

It is well known that hyperventilation, low calcium content of the blood and anoxemia tend to induce epileptic seizures while acidosis high calcium level in the blood and dehydration help to prevent such attacks Induction of these states has been used in the study and diagnosis of epileptic attacks No studies are available on the influence of these conditions on syncope

Hypoglycemic Reactions

Hypoglycemic reactions may closely resemble either syncope or epileptic fits and at present the classification of these attacks is difficult because their exact mechanism is unknown Some persons with reduced glucose content of the blood develop such symptoms as hunger nervousness faintness, dizziness, vertigo, amnesia emotional outbursts delirium, psychosis drowsiness anxiety perspiration rapid pulse lowered blood pressure, diplopia and central scotoma singly or in various combinations At times unconsciousness or convulsions may be the only manifestation Unconsciousness may last from a few minutes to several hours Onset may be gradual or sudden During such attacks of unconsciousness the pulse usually is rapid but the level of the blood pressure shows considerable variation Attacks of collapse and convulsions can be induced in animals through experimental hypoglycemia and some authors claim that these manifestations are of medullary origin Both in animals and in man the level of the glucose in the blood associated with collapse and convulsions varies considerably In many persons these manifestations develop when a glycemia of 0 04 to 0 05 per cent or below is reached I have however, seen a child with such a low level of blood sugar that both the Benedict and the Folin reagents showed no change in color, nevertheless the patient remained practically symptom free

Hypoglycemic reactions may result from inanition or from overexertion, or from the combined effects of these conditions They also occur at times in patients with primary muscular dystrophy The most frequent cause of hypo

glycemic reactions however is induced hyperinsulinism At times spontaneous hyperinsulinism such as occurs in patients with dysfunctions adenoma or carcinoma of the islands of Langerhans in the pancreas may be responsible for the attacks The detailed clinical aspects of this problem are discussed elsewhere in this System (vol 4 chapter V–B) Administration of glucose is specific in these attacks and this therapeutic test may be used as an aid in the diagnosis

Narcolepsy and Catalepsy

Narcolepsy and catalepsy are considered by some as epileptic variants The suddenness of the attacks of irresistible sleep lasting for several minutes together with the cataleptic state frequently present may simulate certain forms of syncope The facts however that these attacks are usually brought on by laughter (Lachschlag) and that the patient often prepares for sleep and lies down instead of collapsing on the ground the sleep like rather than unconscious state the normal blood pressure and cardiac action should make the differentiation definite In doubtful cases the administration of ephedrin should be used as a differential test

Migraine

When migraine is present in its typical form it offers no difficulty in diagnosis The hereditary tendency the hemicranial headache often with onset in the morning the well known visual disturbances and the relatively long duration of the attacks leading to nausea retching vomiting and dehydration make the diagnosis clear in the majority of cases Often however migraine presents a clinical picture closely resembling that of some other condition In an appreciable number of instances the symptoms are mainly or entirely abdominal The attacks may be of short duration with rapid onset The sudden prostration with giddiness muscular weakness abdominal pain and temporary aphasia may simulate certain forms of syncope In addition the patient often appears pale or ashy gray and dehydrated

In the vestibular vertiginous forms of migraine the patient may experience attacks of profound giddiness vertigo ataxia collapse and vomiting Such attacks closely resemble true Meniere s disease and also syncope It is characteristic however that consciousness is retained In the diagnosis of such atypical forms of migraine the history is the most valuable aid A carefully analyzed history often reveals that at one time the attacks were associated with hemicranial headaches eye symptoms or other more specific manifestations In other instances it discloses the fact that other members of the family have suffered from typical

attacks of migraine I have seen two families on the other hand, in which all members suffered from the abdominal type of migraine several members of both families had been explored for appendicitis but the attacks continued At times migrainous attacks of childhood which have been absent for decades, return in modified form after the age of 50 and the interpretation of such attacks also may be difficult As patients suffering from migraine often are sensitive, emotional individuals with vasomotor instability they frequently have a tendency to faint Hence fainting and migraine attacks may occur in the same person

Ménière s Disease

This condition may be confused with syncope particularly if the attacks are severe The presence of deafness marked tinnitus and nystagmus, the severity and duration of the vertigo as well as the finding of lesions involving the labyrinth are helpful in the differentiation In the majority of instances of Meniere s disease consciousness is retained even when the patient is unable to move as a result of the paralyzing vertigo in rare instances however there is transient unconsciousness In the intervals between attacks the diminished Barany caloric reactions on the affected side are also of great assistance Meniere s syndrome may occur as a result of other types of lesions than that of the labyrinth

Neurosis

It has been stated that patients with neurosis frequently suffer from syncope In the majority of instances this type of syncope with or without hysterical manifestations, depends on a definite physiologic mechanism In the discussion of the vasovagal and cerebral type of carotid sinus syncope as well as of the syncope due to pulmonary or cerebral engorgement it has been pointed out that the cardiovascular changes may depend primarily on psychogenic factors These examples are striking illustrations of the fact that manifestations of neurosis not only may imitate visceral changes and syndromes of somatic origin but also may depend on identical changes such as those of organic origin There are instances, particularly during hysterical episodes when patients consciously or subconsciously simulate fainting A careful study of the patient will eliminate difficulty in recognition of such simulation of true syncope

Syncope Collapse and Shock

There are no characteristic features which permit a sharp differentiation between ' vasomotor collapse so called and syncope The marked decrease in

the venous return blood flow the small pulse pressure the fall in the arterial pressure the ashy gray color of the skin the cold perspiration and the decreased or abolished reflexes are cardinal manifestations both of syncope and of vasomotor collapse or shock The difference between these two conditions is quantitative rather than qualitative Syncope results from more sudden changes in the cardiovascular system than are present in collapse Recovery from syncope also is more rapid The presence or absence of consciousness and a rapid or slow cardiac rate cannot be used as differential features because the variant manifestations of syncope often are associated with maintenance of consciousness and rapid heart rate and contrariwise in collapse consciousness may be abolished Clinical evidence strongly favors the concept that syncope vasomotor collapse and shock are closely related conditions varying mainly in degree and duration Such a belief indeed is not original for the celebrated surgeon Travers [3] claimed in 18 6 that syncope and shock differ in degree rather than in kind

In the light of recently acquired knowledge the Roman crucifixion may be used as a striking example of one of the bodily states which may be associated with syncope collapse or shock alone or in combination Renan [4] the great French biblical scholar, in his classic work quotes Roman and Arabic texts bearing on the manner of death by crucifixion The cross was composed of two beam tied in the form of the letter T It was raised slightly so that the feet of the condemned almost touched the earth Frequently a small piece of wood was placed under the feet to prevent the victim from sliding to the ground The extremities though often nailed were sometimes bound with cords If nailed the bleeding was no appreciable factor in the causation of death for it soon stopped Renan claims The real cause of death was the unnatural position of the body which brought on a frightful disturbance of the circulation terrible pain in the head and heart and finally cramping of limbs Victims of strong constitution could even sleep and would die simply of hunger Thirst was a frequent symptom Others died within one or two hours The fact that the victims were allowed to consume wine freely before the crucifixion not only helped to alleviate their sufferings but in addition the vasodilator and blood pressure reducing effect of alcohol must have been a contributory factor in the induction of rapid fainting or vasomotor collapse

The observations made on tilted subjects and animals as well as the present knowledge of collapse and shock entirely support the rationale of such description and explanation It is known that when certain mammals are tied on a board and are held in an upright position they rapidly go into shock and die We have also indicated that if normal subjects are held motionless on a tilting table in the upright position the pulse pressure progressively decreases often with a maintained or even an elevated diastolic pressure The heart rate becomes

more and more rapid, the pulse more feeble The veins appear collapsed The subject becomes drowsy and yawns and sighs frequently Some subjects can stand this condition for a long time others may go into a 'dead faint' within a short period The latter is regularly the case if a vasodilator substance such as nitrite is given If the subject is not returned promptly to the horizontal position, such a faint may well become serious, as must often have been the case with those crucified According to the best sources of information, quoted by Renan, death occurred suddenly when the subject appeared strong a few moments before Renan offers the explanation that apoplexy, or "instantaneous rupture of a vessel near the heart", caused such sudden death It is more plausible, from what we know today, that a fatal faint or collapse ended the suffering

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CHAPTER IX

DISEASES OF THE PERICARDIUM

By C. SIDNEY BURWELL

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heart within it are active and constant On the basis of the experimental observations of Kuno[45] and others it is considered by many that the pericardium serves to limit the diastolic dilatation of the heart and that thus it has a useful protective function While it is true that under experimental conditions excessive dilatation is produced more easily when the pericardium is open it is true also that people with large congenital defects of the pericardium live essentially normal lives Perhaps the suggestion in the literature that patients with absence of the pericardium frequently have slightly hypertrophied hearts may emphasize this possible function of the pericardium

The pericardium appears also to guard the surface of the heart from the extension of infection from neighboring organs Infection may exist in the adjacent pleura for example without invading the pericardial sac

Pain is a frequent accompaniment of acute inflammation of the pericardium The sensibility of this serous membrane has been studied in man by Capps[15] who introduced wires into the cavity by way of needles and by Alexander MacCleod and Barker who studied a pericardial cavity exposed by an operation for suppurative pericarditis Capps observed that stimulation of the parietal pericardium near its diaphragmatic attachments produced pain in the homolateral side of the neck in the *region of the trapezius He inferred that this portion of the pericardium* is like the adjacent diaphragmatic pleura supplied with afferent fibers of the phrenic nerve Stimulation of the parietal pericardium above this point failed to produce pain Stimulation of the epicardial surface failed to induce *a pain response Capps concludes* The presence of pain with pericarditis usually indicates the involvement of the tissues outside the pericardium especially the pleura Pleuropericarditis may create a variety of pain complexes depending on the location of the disease Anterior mediastinitis by involving the parietal pleura causes direct local pain aggravated by inspiration and with tenderness on pressure A pleuropericarditis near the attachment to the diaphragm with or without involvement of the *diaphragmatic pleura* gives rise to pain in the neck by way of the phrenic nerve Posterior mediastinitis may involve the parietal pleura and cause dorsal pain Pleurisy is a common complication of the pericarditis in pneumonia and rheumatism whereas it is infrequent in the pericarditis of nephritis and other terminal diseases This probably explains the painless character of the nephritic pericarditis and the relatively painful picture commonly attributed to the rheumatic type

Capps studies were made in patients with pericardial effusion re

Introduction

Disease of the pericardium may lead to disability or death either because the disease process itself is progressive or because the changes produced by it interfere with the normal working of the heart. These disorders are worth attention also because disease processes in this secret recess are overlooked frequently. Before embarking upon a consideration of the problems presented by disease a few observations may be made concerning the structure and function of the pericardium.

Anatomy of the Pericardium

The pericardium is a closed sac of fibrous tissue and serous membrane surrounding the heart and extending along the proximal portions of the great vessels. The fibrous outer layer is anchored firmly to the central tendon of the diaphragm and bound loosely to the sternum in front and the structures of the mediastinum behind. This fibrous layer is thick and resistant enough to permit the piling up of intrapericardial pressures of several hundred millimeters of water. Under pressure however it has the capacity for slowly stretching and increasing the size of the pericardial cavity several fold. Wallraff[64] makes the interesting comment with a teleological flavor that the fibrous wall of the pericardium is thick where the muscular wall of the heart is thin.

The serous layer lines the fibrous one and is reflected over the surface of the heart where it is closely applied to the muscle and the coronary vessels. Between the parietal and visceral layers is the potential pericardial space. The layers extend along the great vessels enclosing the aorta and pulmonary artery in a common sheath. Between this sheath and the auricles lies the so called transverse sinus. There is a nearly comparable reflection over the pulmonary veins and the superior vena cava and a smaller one over the inferior cava.

Physiology of the Pericardium

The pericardium is part of the body irrigated by blood traversed by lymphatics and supplied with nerves. During life the movements of the

changes usually will supply an adequate basis for the planning of treat ment

In discussing disease of the pericardium it is convenient and time saving to reverse the order of these headings Accordingly we begin with

The Changes Produced by Disease of the Pericardium in the Function of Organs

Tamponade

An important result of many instances of pericardial disease is interference with the movements and function of the heart An understanding of the mechanism called *cardiac tamponade* is necessary to an understanding of this interference and to an explanation of many of the signs and symptoms of pericardial disease Beck[5] prefers the term cardiac compression to tamponade A strict definition of tamponade or cardiac compression would limit it to an interference with the filling of the heart by pressure from without Such pressure may be exerted by fluid or solid masses Without too much etymological violence the definition may be widened to include the interference with the filling of the heart which may be imposed by a thickened pericardium

The concept of cardiac tamponade is not new When Dr Nicholls[54] wrote in 1760 to the President of the Royal Society concerning the post mortem examination of the body of King George the Second he indicated his understanding of the mechanism of tamponade in these words

upon examining the heart its pericardium was found distended with a quantity of coagulated blood nearly sufficient to fill a pint cup and upon removing this blood a round orifice appeared in the middle of the upper side of the right ventricle of the heart large enough to admit the extremity *of the little finger Through this orifice* all the blood brought to the right ventricle had been discharged into the cavity of the pericardium and by that extravasated blood confined between the heart and pericardium the whole heart was very soon necessarily so compressed as to prevent any blood contained in the veins from being forced into the auricles which therefore with the ventricles were found absolutely void of blood either in a fluid or coagulated state

As therefore no blood could be transmitted through the heart from the instant that the extravasation was completed so the heart could deliver none to the brain and in consequence all the animal and vital motions as they depend on the circulation of the blood through the brain must necessarily have been stopped from the same instant and

quiring paracentesis the stimulus was a mechanical one i e poking with a silver wire introduced through the needle Alexander MacLeod and Barker studied a pericardial cavity which was exposed for some sixteen days after an operation Over the ventricles most forms of stimulus were felt as touch The parietal pericardium gave a sensation of pressure when pressure was applied to the surface of its posterior and left postero lateral walls Pressure forward against the anterior pericardium produced severe local pain spreading toward the axilla and the epigastrium Irrigation of the pericardial cavity was often accompanied by coughing

Normally a minimal amount of fluid exists in the pericardium and under several conditions inflammation alteration in the dynamics of the circulation hemorrhage and perhaps others this amount may be increased the volume may become great enough to increase the intrapericardial pressure and to interfere with the normal movements of the heart Little is known about the factors controlling the accumulation and absorption of fluid in the pericardium Drinker and Field[59] observed that in the rabbit s pericardium lymphatics are not numerous except toward the base Serum injected into the pericardial cavity was removed by the lymphatics but only very slowly in spite of the movements of the heart which might be expected to encourage resorption Blalock Cunningham and Robinson[10] have reported experiments in which ligation of the superior vena cava was followed by the development of chylothorax and chylo pericardium Observations on the absorptive powers of the human pericardium have been made by Stewart Crane and Deitrick[61] in a patient with recurrent pericardial effusion and therefore with a pericardium probably not normal They showed that phenolsulphonpthalein disappeared rapidly from the pericardial cavity while vital red which has a larger molecule remained for much longer periods They considered these observations to be in harmony with those of Drinker and Field in the rabbit as indicating the slowness of absorption by way of the lymphatics

Disease of the Pericardium

Disease of the pericardium is considered conveniently under the headings made familiar by the current classification of heart disease recommended by the American Heart Association These headings are (1) the *causes* of disease (2) the changes produced by disease in the *structure* of organs and tissues and (3) the changes produced by disease in the *function* of organs The description of a given case of pericardial disease in terms of its etiology the morphological changes and the functional

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The Changes Produced by Disease of the Pericardium in the Function of Organs

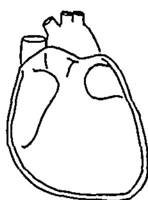
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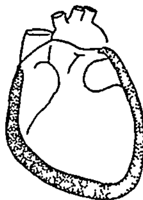
An important result of many instances of pericardial disease is interference with the movements and function of the heart An understanding of the mechanism called *cardiac tamponade* is necessary to an understanding of this interference and to an explanation of many of the signs and symptoms of pericardial disease Beck[3] prefers the term cardiac compression to tamponade A strict definition of tamponade or cardiac compression would limit it to an interference with the filling of the heart by pressure from without Such pressure may be exerted by fluid or solid masses Without too much etymological violence the definition may be widened to include the interference with the filling of the heart which may be imposed by a thickened pericardium

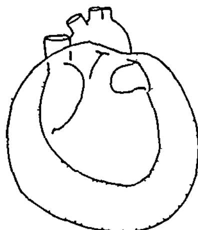
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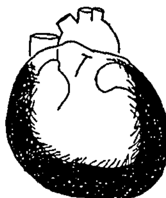


FIG 1 Diagram showing the relation of heart and pericardium in the normal and in patients with tamponade In the ca e of sudden hemopericardium the heart is slightly maller and the pericardium slightly larger than normal in that of ubacute effu ion the heart is slightly smaller and the pericardial sac con iderably larger than normal in that of chronic constrictive pericarditis the heart may be smaller than normal the pericardial cavity is obliterated and both layers of the pericardium are greatly thickened (Thi illu tration is taken from an article by Burwell and Blalock by permis ion of the Journal of the American Medical Association)

his Majesty must therefore have dropped down and died instantaneously

Chevers[19] who published his famous description of constrictive pericarditis in 1842 clearly appreciated that compression of the heart can result from a constricting pericardial scar

The use of the term and the modern discussion of the mechanism

begin in the latter part of the nineteenth century Rose[59] in 1883 in an article entitled Herztamponade ein Beitrag zu Herzchirurgie reported a number of traumatic affections leading to the accumulation of blood in the pericardium and the production of a group of symptoms and signs which he believed characteristic of the condition

In 1877 a little before Rose s publication the classical experiments of the physiologist Cohnheim illuminated the problem of tamponade[70] Cohnheim injected fluid (oil) into the pericardium of animals and observed that as the intrapericardial pressure rose there was a rise in general venous pressure a fall in systemic arterial pressure and a diminution in the ventricular output He concluded that an impediment to the filling of the cavities of the heart is brought about by every effusion of fluid into the cavity of the pericardium which is capable of causing a certain degree of tension of its wall Cohnheim was aware also that aneurysms or other mediastinal tumors sometimes may oppose an obstacle to the entry of blood into the heart and lead to the development of the phenomena of tamponade In more recent times the study of patients with constrictive pericarditis has revealed that in this condition the thick and contracted scar tissue which replaces the relatively distensible pericardial structure may limit the diastolic dilatation of the ventricle and thus reproduce the essential mechanism of tamponade The study of such patients who offer particular opportunity for measurements of the circulation has thrown light upon the phenomena of tamponade The information available up to 1938 was summarized by Burwell and Blalock[17]

They based their conclusions chiefly upon the observations of a group of patients with constrictive pericarditis but it is under tood that these conclusions in so far as they relate to the peripheral circulation and not to the signs in the heart may be applied also to tamponade from fluid They found the alterations in the circulation to have many similarities to those of heart failure but they observed important differences also and it is emphasized that tamponade is different from heart failure in genesis course and treatment Some of the results of the studies were as follows

1 *The peripheral venous pressure* is high from 150 to 390 mm of water by a method[59] which in normal persons usually shows readings of 50 to 100 mm of water This pressure fluctuates somewhat but remains high more persistently than does the venous pressure of patients with myocardial failure It is illuminating to observe that the pressures in arm and leg are not notably different unless the leg pressure is elevated by the presence of ascites This similarity implies that the obstruction to

the entry of blood into the heart is to be found not in a constriction of the great veins but in a failure of the heart to dilate normally

2 *The peripheral arterial pressure* usually is low the systolic pressure with the patient at rest is most often from 90 to 110 mm of mercury The pulse pressure usually is between 15 and 25 mm of mercury which is low as compared to that of normal people and the pulse is correspondingly small During inspiration the arterial pressure falls and the already small pulse becomes still smaller and may cease to be palpable

3 *The basal heart rate* is higher than in normal persons In these patients it lay between 80 and 106 beats per minute

4 *The movements of the heart* are diminished as they are observed by fluoroscope and x ray kymogram The reduction in the excursion usually is most obvious on the right border of the heart shadow

5 *The total blood volume* in the two cases in which it was studied was from 30 to 45 per cent above the calculated normal

6 *The arm to tongue* and *arm to carotid time* is prolonged i e the velocity of blood flow is diminished

7 *The output of the heart per minute* and *per beat* is diminished As compared with a normal of ± 3 87 liters the output per minute in these patients usually is about 2 liters The blood expelled per beat is diminished in all cases The normal is on the average about 64 c c in these patients it is from 18 to 40 c c Moreover contrary to the normal this stroke volume does not increase significantly during exercise

The manifestations of constrictive pericarditis thus include changes in venous pressure which are similar to those in congestive heart failure and changes in cardiac output and arterial pressure which are somewhat similar to those observed in patients with circulatory collapse

Similar changes in cardiac output and venous pressure were observed by Stewart Crane and Deitrick[6] in a patient with recurrent pericardial effusions

Tamponade of the heart whatever its cause produces a set of manifestations which usually is recognizable These manifestations in the main are attributable to the dynamic changes just described

A patient with tamponade may be expected to show marked venous engorgement This can be seen most easily in the neck the arms and the retina and is more striking in thin people It is particularly marked in those patients who have had venous hypertension for weeks or months and thus is apt to be more impressive in patients with tuberculous constrictive pericarditis than in those with a stab wound of the heart The veins are not only visibly distended but are also firm to the touch The liver is enlarged but does not pulsate When the condition is one of

long standing there may be ascites pleural effusion and edema Some patients exhibit ascites earlier than *or out of proportion to other collections of fluid The heart rate is rapid but usually regular* the pulse is small quick and paradoxical The paradoxical quality sometimes may be recognized during the measurement of arterial pressure when it is not apparent to the finger Dyspnea on moderate or slight exertion is the rule severe dyspnea at rest is noted seldom in the absence of large pleural effusions Weakness is a usual complaint and fatigability

Tamponade then is characterized by an interference with the filling of the heart When patients die as they may from tamponade they do so *from increasing obstruction to filling and increasing disturbance of the movement and distribution of blood The final collapse of the circulation* usually is preceded by rising venous pressure and progressive fall in arterial pressure the latter is a danger signal to be watched for attentively Tamponade is produced most commonly by hemopericardium by pericardial effusion or by constrictive scar

It has been emphasized that tamponade interferes mainly with the filling of the heart and produces the so called Einfluss stauung Pericardial disease may lead also to interference with the contraction and emptying of the heart Here *we are on ground much less firm since we lack measurements to support this contention* but a glance at Fig a photograph of the heart of a patient dying with severe tuberculous pericarditis makes it seem probable that such masses of inflammatory tissue may interfere with both filling and emptying A difficulty in emptying may be a factor also in those patients who as a sequel to acute rheumatic fever or possibly other conditions suffer from the so called *mediastinopericarditis*

In this form of chronic pericarditis mediastinopericarditis the heart is bound by adhesions to neighboring structures some of which may be firmly placed and relatively unyielding It is assumed partly on the evidence of observations of the surface of the body or of the shadow of organs with the fluoroscope that each systole requires the forcible displacement of some of these structures e g the inward displacement of ribs or an upward tug on the diaphragm It appears not unreasonable to conclude that such displacement requires extra *work on the part of the heart and that this extra work may be a factor in hypertrophy and sub*sequent failure of the heart It is difficult to decide how valid or important these conclusions are since this variety of pericarditis usually is associated with valve disease At any rate it seems according to the present rather scanty evidence that in these patients there is no great impediment to filling the difficulty appears to be cardiac overload due to



Fig 2 The heart and portions of the lungs of a patient with extensive caseous tuberculosis of pericardium and mediastinum (This illustration is taken from an article by Burwell and Blalock by permission of the Journal of the American Medical Association)

an interference with emptying and leading to myocardial exhaustion and failure This failure apparently does not differ in nature from heart failure following chronic myocardial or valvular disease

Extracardiac Compression

These disturbances in filling and emptying of the heart and the consequent changes in the amount and distribution of blood are the major changes in the function of organs resulting from cardiac disease One might mention also the compression of the lung and the interference with its movements which may result from massive pericardial effusions Such effusions also may displace the esophagus As a result of such changes there may be cough hoarseness difficulty in swallowing and alterations in respiration

Electrocardiography

The changes of disease whether they be exudative or proliferative may extend beyond the tissues of the pericardium itself and give rise to symptoms and signs originating in adjacent structures The frequency of pleural involvement and pain in association with acute pericarditis has been mentioned Examination of the tissue adjacent to the visceral pericardium i e the myocardium may also reveal involvement in association with disease of the pericardium The hydrostatic pressure of pericardial fluid may lead to myocardial ischemia or such fluid conceivably may act to damp electric impulses originating in the heart At any rate some mechanism perhaps one of these produces alteration in the electrical phenomena associated with the heart so that patients with pericardial disease often exhibit changes in the electrocardiogram These changes are observed in pericarditis with effusion and also in the constrictive form The same general changes appear in both and consist in the main of (1) changes in the height of the QRS complex and (2) changes in the T waves Low voltage (i e small complexes) is frequent and flattening or inversion of the T waves usually appears also Either type of change may appear without the other These changes are somewhat similar to some of those that may appear in coronary occlusion pulmonary infarction rheumatic carditis myxedema or after the administration of digitalis White[67] has the following points to make regarding the relation between the electrocardiogram in pericarditis and in coronary disease The S-T interval and T wave changes resemble to a certain extent those found in coronary disease especially those in acute occlusion namely a low origin

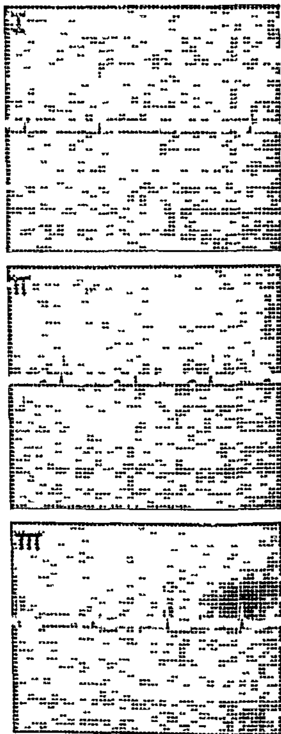


FIG 3 Electrocardiographic tracings from a patient with constrictive pericarditis. They show inverted T waves and small complexes

of the S–T interval with flattening or inversion of the Ts (T waves) there are however two distinct differences (1) the T wave changes are usually consistently found downwardly directed in all three classical leads in contrast to the opposite direction of T_1 and T_3 after coronary throm

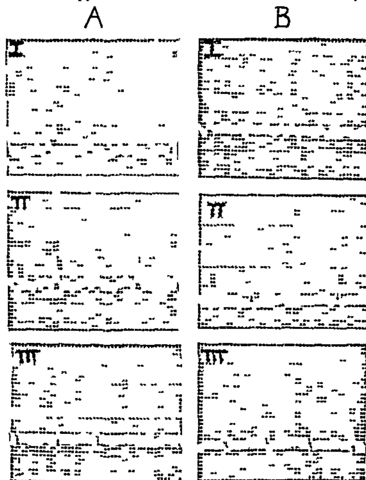


FIG 4 Electrocardiographic tracing from a patient with rheumatic pericarditis with effusion A Taken before paracentesis shows rather small complexes inverted T waves in all three leads and tachycardia B Taken some hours after the removal of 1500 c c of fluid shows a change toward the normal in the direction of the T waves but no other marked alteration

bosis and (2) the Q waves are not exaggerated in pericarditis as they are in either lead 1 or lead 3 after acute coronary occlusion

An excellent analysis of the electrocardiographic changes associated

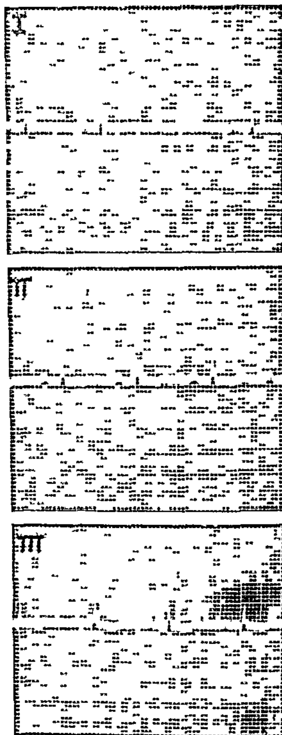


Fig. 3 Electrocardiographic tracings from a patient with constrictive pericarditis. They show inverted T waves and small complexes

sively or simultaneously fibrinous exudate extensive effusion constricting pericardial scar calcification Since the visceral pericardium is applied closely to the myocardium and in intimate functional relation with its blood supply and metabolism it is not surprising that affections of the pericardium often involve the superficial layers of the heart muscle and vice versa To a less degree the same may be said of the structures immediately outside the parietal pericardium The following varieties of pericardial abnormality warrant description

Deficiency or Absence of Pericardium

Disturbance of development may result in the absence of large or small areas of the pericardium Complete absence is very rare and usually associated with grave congenital heart disease such as ectopia cordis Partial deficiency is rare enough to be notable it is usually in the left side of the sac Absence of even large portions of the pericardium seldom is recognized during life An exception is Ladd s[46] case which occurred in a patient with a diaphragmatic hernia and was recognized during an operation for the relief of that condition Beck[4] has considered patients with deficiency of the pericardium as throwing light on the problem of pericardial function He studied the records of reported cases and found two noteworthy facts adhesions between the heart and adjacent organs were more frequent than when the pericardium is present and there was no evidence that deficient pericardium exerted a significant influence on the patient s health or length of life Crynes and Hunter[27] describe escape of the heart from the pericardial sac when the pericardium has been ruptured by trauma usually severe compression of the chest The split in the membrane usually is on the left side

Southworth and Stevenson[61] have made a careful compilation of the available information concerning congenital defects They report a patient exhibiting absence of the left leaf of the pericardium with an interpleural window in the anterior mediastinum and they find in the literature no less than 45 other instances of this defect These points may be made in most of the cases (76 per cent) the heart and left lung were in a common serous cavity in 27 per cent of the cases death was associated with pleuro pericarditis

Diverticula of the Pericardium

Hernia like out pouchings of the pericardium are encountered Cushing[23] in 1937 reported an analysis of 40 cases one of his own and

with pericarditis was published by Noth and Barnes[56] in 1940. They describe certain differences in the electrocardiographic curve as between acute and chronic pericarditis. In the former there is often elevation of the S-T segment and there may be, especially in the early stages, exaggerated T waves in the standard leads. In chronic constrictive pericarditis, on the other hand, the T waves usually are flat or inverted and the QRS complexes small.

Electrocardiography occasionally may actually suggest the diagnosis of pericardial disease. Probably these paragraphs are more needed, however, to point out that these alarming reductions in voltage and aberrations in the T wave are consistent with the diagnosis of pericarditis and may even disappear when the pericardial disease heals.

In patients whose pericardial disease is part of a rheumatic condition there may be also transient and variable defects in A-V conduction due of course to associated lesions of the myocardium and not to the pericardial disease per se.

An interesting application of electrocardiography to the diagnosis of pericardial disease was made by Dieuaide in 1922[28]. He showed that when the heart is anchored by extensive adhesions its fixation may often be demonstrated by the failure of the electrical axis to change to a normal degree with change of position of the patient. Further cases have been studied by Sampson and Rosenbloom[60]. They point out that shift of the axis may occur in patients with mediastinopericarditis of considerable degree. Fixation of the axis, however, is good evidence of fixation of the heart; occasionally such fixation of the heart may be due to factors other than mediastinopericarditis.

* * *

We have considered the changes in the function of organs brought about by disease of the pericardium. Attention may now be turned to a consideration of pericardial disease from the morphological point of view.

Changes in Structure Associated with Disease of the Pericardium

The pericardial structures briefly described in early paragraphs may respond to injurious influences with a variety of changes. It should be understood now that there is no parallelism between morphological types and etiological types of pericardial disease. In the course of tuberculous pericarditis, for example, the morphological alterations may be succes-

two of its properties namely its striking superficiality and its cross times with the valvular sounds The rub single or double is around about these sounds rather than coincident with them If complete it consists of three parts — the systole of the auricle and the systole and diastole of the ventricle Moreover on shifting the stethoscope the rub obeys none of the boundaries nor the lines of propagation of the valvular murmurs Inconstant as it is yet it frequents the middle and basic areas of the heart centering usually about the second and third intercostal spaces and neighboring sternum and being conducted beyond its primary seat ends here this seat may however be a wide one it may sound over the whole of the chest or at the xyphoid dying out towards the apex occasionally in a rheumatic case it may be heard behind especially if the left lung be collapsed and the heart large not so rarely in Bright s disease in which the rub is apt to be harsher and more persistent The intensity of the sound is no guide to the degree of inflammation in Bright s disease the patch is often a small one and more or less stationary The friction sound may be increased by pressure with the stethoscope especially in the softer chests or may vary with change of position such as leaning forward or from hour to hour or again with the respiration increasing on deep inspiration sometimes on deep expiration

When the rub is loud it may be possible to note a palpable friction also

Fluid within the Pericardium

Many of the results of the presence of a considerable volume of fluid within the pericardium are in general similar whether the fluid be blood transudate serous effusion pus or even gas The manifestations include (1) the evidences of tamponade (2) physical signs revealed by the examination of the heart itself (3) other signs chiefly having to do with the disease process leading to the presence of fluid

(1) The manifestations of tamponade are enumerated on a previous page in the section with that heading These manifestations even in high degree may appear when the pericardium contains as little as 250 to 400 c c of fluid if this appears suddenly as in rupture of the heart or if some influence such as a sub acute pyogenic infection has led to a thickening of the pericardium and an increase in its resistance to stretching This occurrence of symptoms of severe obstruction with a relatively small volume of fluid is due as was observed by Cohnheim to the fact that it is the *pressure* within the sac rather than the *amount* of fluid which determines the degree of interference with the entry of blood into

39 collected from the literature He concluded that these diverticulæ may occur as congenital malformations or as the result of pressure or traction Diagnosis seldom is made or required unless some additional factor is present In his own case for example the diverticulum was the seat of tuberculous inflammation and filled with fluid It projected from the anterior chest wall and the appearance suggested aneurysm or cyst The x ray film may suggest similar conclusions concerning diverticulæ which do not protrude externally The connection of a diverticulum with the pericardium sometimes may be demonstrated by injecting air into the suspected cavity and watching it enter the pericardial sac

Fibrinous Pericarditis

A fibrinous exudate on the pericardial surface occurs in many varieties of inflammation including those produced by rheumatic fever tuberculosis infection with pyogenic cocci or chronic nephritis The exudate may be thin and dry or thick and buttery it may be local or general The movements of the heart lead to various patterns in the arrangement of fibrin over the pericardial surface The appearance may be described as shaggy or hairy or as resembling bread and butter honeycomb or tripe Fibrin often collects in masses in the auriculo ventricular groove this may be the reason why particularly heavy scar tissue sometimes is found in this region later

The condition is often overlooked Attention may be called to it by pain but the diagnosis is made by the presence of the characteristic friction rub usually the sole and always the sole reliable sign This rub may be loud and creaking or soft and whispering It is notoriously evanescent and variable and the houseofficer who proudly offers it as his contribution to an obscure diagnosis sometimes is not able to demonstrate it to his visiting man It has one characteristic of real importance in its recognition usually it is audible both in systole and diastole It often sounds close to the ear and occasionally it may be increased by pressure Sometimes it cannot be differentiated finally from an endocardial murmur except by waiting a few days The following description by Allbutt taken from his original chapter in the Oxford Medicine is admirable

Friction then may be harsh and persistent or elusive and transient, so that from its absence little or nothing can be inferred When present it is easy of apprehension though variable in quality position and degree It has been compared with creaking leather with rustling silk with crackling parchment How then can it be easy of recognition? By

fibrinous exudate on the surface In such cases a friction rub usually is heard also after the effusion has developed in spite of a widespread superstition to the contrary Indeed when one suspects from other signs that pericardial fluid is present he may feel sustained or at least supported by finding a friction sound Conner [1] observed a friction sound in 70 per cent of 34 cases at times when signs of fluid were present

Fluid in the pericardium frequently is accompanied by signs at the left lung base Ewart s sign These are spoken of often as signs of compression but they occur in association sometimes with relatively small effusions Dulness and bronchial breathing below the left scapula are the main signs and may be so marked as to suggest pneumonia Occasionally these signs are bilateral It is considered by Gevalt[26] that these signs occur almost exclusively in rheumatic pericardial effusion and he suggests that they are due to some specific effect of this condition perhaps a pneumonitis rather than to compression from fluid The unilateral character of the sign and the fact that it may change promptly with change of position casts some doubt on his tentative explanation

Aside from the pain which often is severe the symptoms of pericardial effusion per se are on the whole symptoms of the tamponade An exception is a troublesome spasmodic cough which is seen more frequently in rheumatic pericarditis with effusion than in other varieties It will be recalled that the injection of irritating fluid into the pericardial cavity may be followed by similar coughing

The dyspnea of pericardial effusion is a complex phenomenon factors in it may include reduction in vital capacity (itself brought about by accumulation of fluid in pericardial pleural and peritoneal cavities and by change in pulmonary and peripheral circulation) compression of lung areas displacement of mediastinum and painful inflammation of the pleura This dyspnea in large effusions may be severe and troublesome

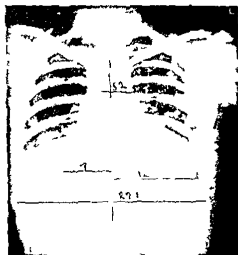
Occasionally the disturbance of the circulation is so great that cyanosis results probably chiefly on the basis of great diminution of blood flow Large effusions may produce enough pressure on and perhaps displacement of the esophagus to cause dysphagia

(3) Obviously the occurrence of signs of disease processes such as pneumonia acute rheumatic fever or glandular tuberculosis which may be concerned etiologically is of importance in the diagnosis of pericardial effusion

The indications for paracentesis in cases of pericardial effusion will be considered later but here we may mention certain special types of fluid in the pericardium and also the examination of fluid obtained by paracentesis from the pericardium

the heart When fluid accumulates more slowly and when the membrane is not unusually resistant very large amounts of fluid 1 000 c c to 2 000 c c or even more may be found within the *pericardium* There is then no strict relation between the amount of fluid and the severity of the signs of tamponade Immediately after *removal of fluid* by tapping or during the period of its resorption there may be for obvious reasons only slight signs of tamponade although a considerable volume of fluid still is present

(2) Fluid in the pericardium often brings about a diminution in the audibility of the heart sounds and a diminution or even absence of its palpable and visible pulsations The cardiac dulness is increased in extent and changed in shape becoming convex outward on both sides



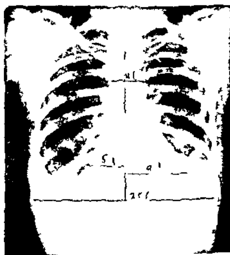


FIG 5 Anteroposterior *films of patient* with pericardial effusion A One day after admission B Sixteen days later

The x ray may show a corresponding shadow often larger than one expects in which the normal landmarks of the cardiac silhouette are obliterated When only *small* amounts of fluid are present it may show as an increased density at the *lower corners* of the heart shadow Sometimes a change in the *position of the fluid* when the patient changes from the *upright to the recumbent* position may lead to a change in the shape of the shadow usually a *widening* at the upper portion of the shadow Under the fluoroscope the *pulsations* are obscured and appear reduced or *absent* It should be remembered that fluid may be encapsulated and cause a localized bulging

Of course inflammatory pericardial effusion is often preceded by a

fibrinous exudate on the surface In such cases a friction rub usually is heard also after the effusion has developed in spite of a widespread superstition to the contrary Indeed when one suspects from other signs that pericardial fluid is present he may feel sustained or at least supported by finding a friction sound Conner[21] observed a friction sound in 70 per cent of 34 cases at times when signs of fluid were present

Fluid in the pericardium frequently is accompanied by signs at the left lung base Ewart's sign These are spoken of often as signs of compression but they occur in association sometimes with relatively small effusions Dulness and bronchial breathing below the left scapula are the main signs and may be so marked as to suggest pneumonia Occasionally these signs are bilateral It is considered by Gevalt[35] that these signs occur almost exclusively in rheumatic pericardial effusion and he suggests that they are due to some specific effect of this condition perhaps a pneumonitis rather than to compression from fluid The unilateral character of the sign and the fact that it may change promptly with change of position casts some doubt on his tentative explanation

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Hemopericardium

Blood in the pericardial cavity is found under a variety of circum stances In civil life it is often the result of rupture of an aneurysm saccular dissecting or mycotic or of the ventricular muscle usually as the result of extensive infarction In war or population groups in which knives or daggers are usual weapons of controversy penetrating wounds of the heart are not especially rare That this is a matter of customs rather than race is indicated by the fact that some of the larger series of such cases occur in such diverse areas as the southern United States and Finland In these cases as in the case of bullet wounds injury to the heart the coronary arteries or the intrapericardial portion of great vessels can lead rapidly to hemopericardium Non penetrating trauma is a rare cause of gross hemorrhage A special variety of hemopericardium is that observed in some cases of cancerous metastasis to the pericardium when there may be a mixture of serous fluid and blood Mixtures may exist also in scurvy and in some cases of pericarditis from infectious agents The signs of hemopericardium are the signs of fluid but there is one point to emphasize The accumulation of blood in the pericardium often is rapid and may be almost instantaneous Therefore this is the situation par excellence in which severe tamponade may exist with relatively small amounts of fluid Moreover the rapidity of the development means that not only the pericardium but also the veins have not had time to stretch therefore their distension is less apparent grossly than when they have long been exposed to unusual pressures Finally the increase in blood volume that may occur in long standing tamponade is not present For all these reasons the picture is different from a more slowly accumulating fluid mass the heart pericardium area is smaller the veins are less distended and circulatory shock may be a dominant part of the total picture

Pyopericardium

This variety of pericarditis with fluid accumulation is not rare Its prompt recognition is essential because early surgical treatment may be effective and delay may be fatal Pus in the pericardium comes about because pyogenic organisms have become established there The most frequent are pneumococci staphylococci and streptococci They may reach the pericardium by extension from a neighboring organ by blood stream transportation or through penetrating wounds

The picture as one would expect is a combination of the signs of

fluid and those of infection This is a case in which the capacity of the pericardium to stretch may be limited by inflammatory tissue so that the evidences of tamponade may appear with relatively insignificant amounts of fluid A friction rub may occur but usually is absent

The diagnosis may be suspected when a patient with for example pneumonia or osteomyelitis exhibits the evidences of tamponade and the local signs of pericardial fluid the diagnosis is confirmed or disproved by paracentesis Paracentesis and its far from negligible dangers will be discussed later here it may be said that the question of the presence of pyopericardium is one of the few that may justify carrying out of pericardial paracentesis

Special Varieties of Fluid

Chylopericardium

Ligation of the superior vena cava in animals as has been shown by Blalock Cunningham and Robinson[10] may result in the accumulation of chylous fluid in the pericardium and in the pleura Yater[0] describes chylothorax and chylopericardium due to obstruction of the thoracic duct and the upper great veins in his case associated with metastatic carcinoma of the superior mediastinum and thrombosis of the great veins and the mouth of the duct He states that only three cases of chylopericardium had been recorded up to 1935

Cholesterol Pericarditis

Another special variety of fluid is one containing considerable amounts of cholesterol In the case described by Alexander[1] the cholesterol crystals gave an appearance like gold paint to the rather dark colored fluid This patient had many signs of myxedema Merrill's[53] patient with cholesterol pericarditis had similar symptoms and a blood cholesterol of 278 mgm per cent but a basal metabolic rate of +19 per cent The fluid of this kind observed by Daniel and Puder[5] occurred in a patient with pericarditis which probably was tuberculous and that described by Herzenberg and Fafius Gordon[39] in a patient with extensive metastatic carcinoma of the pericardium

In three of these cases the fluid was obviously bloody and it has been suggested that hemolysis of erythrocytes had been followed by absorption of part of the fluid and precipitation of some of the cholesterol which had been present in the bloody fluid

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of the thickness of the pericardium or of the presence of adhesion or localized collections of fluid

Fibrous Pericarditis

During the course of long lasting pericarditis or following the subsidence of acute inflammation areas of fibrous tissue may be observed occurring in relation to the pericardium or replacing it Such fibrous

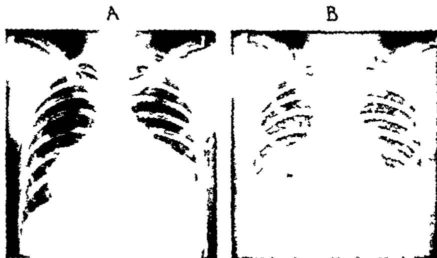


Fig 6 Anteroposterior films of patient with tuberculous pericarditis with effusion *A* Before tapping *B* After removal of fluid and injection of air Notable are the fluid level the relatively small heart in the greatly enlarged pericardium and the thickness of the shadow of the diseased pericardium.

tissue varies in quantity, distribution and its effect on the movements of the heart There may be only small localized areas covered with pericardium or bands of filamentous adhesion or a generalized union of the two layers or thick strata of fibrous tissue replacing pericardium and imprisoning the heart or extensive masses of fibrous tissue joining the heart in firm union to the surrounding structures of the mediastinum The localized spots the filamentous adhesions and the non resistant generalized union of the layers appear to produce no significant disturbance of cardiac function They are the footprints of previous disease but there are no present means of recognizing them during life and they require no treatment There are however two varieties of fibrous pericarditis which may produce disability and one of these varieties may offer an oppor

The Examination of Pericardial Fluid

The recorded literature is practically free of well organized material describing the varieties of fluid occurring in the pericardium There is no adequate knowledge of the formation reabsorption or characteristics of normal pericardial fluid Presumably the methods used in examining pleural fluid may be employed and similar significance assigned to the findings

PNEUMOPERICARDIUM

Gas in the pericardial cavity comes about in several ways (1) spontaneous gas formation from infected fluid (2) traumatic perforation from without (3) perforation of the pericardium by extension of a disease process from a neighboring organ usually esophagus stomach or lung (4) deliberate introduction by way of a needle for diagnosis or therapy or (5) accidental introduction during paracentesis

The condition is rare Liquid as well as gas usually is present This combination is responsible for some of the extraordinary physical signs that lend this condition peculiar interest They also make it recognizable Landis[55] found references to 46 cases and observes In spite of the fact that it has never fallen to the lot of any one man with the exception of Mueller to see more than one example of this condition it is worthy of mention that 40 of the 46 cases were recognized as instances of pneumopericardium before death Use of air injection in the treatment of tuberculous pericarditis with effusion doubtless has given some observers opportunity to study the signs repeatedly

The physical signs that come so near to being pathognomonic are two areas of tympany and dulness in the precordium shifting with the position of the patient and an extraordinary rhythmic churning sound on auscultation This is described sometimes as having a metallic ringing character or as similar to the sound of a mill wheel bruit de moulin or bruit de la roue hydraulique

Occasionally somewhat similar succussion sounds are produced by the motion of the heart in *hydropneumothorax* in this case confusion may arise unless the diagnosis is put to the test of careful physical and x ray examination

The combination of liquid and gas in the pericardium produces an elegant contrast in the roentgenogram which gives a third characteristic finding as shown in Fig 6 The x ray of an air containing pericardium permits determination of the heart size and may even give an indication

TABLE I

INFLUENCE OF ADHESIVE PERICARDITIS ON WEIGHT OF HEART

(Laws and Levine[6])

Valvular lesions	With pericarditis		Without pericarditis	
	Number	Weight	Number	Weight
Aortic	3	663	8	671
Mitral	9	449	11	47-
Aortic and mitral	16	761	17	564
Mitral and tricuspid	7	607	6	495
Aortic mitral and tricuspid	8	706	20	498
Total	43	654	62	534

to be suspected in patients with multiple valve disease of rheumatic origin especially in the presence of a very large heart Fixation of the heart in relation to the thorax as shown by absence of normal shift of the apex beat the dulness the fluoroscopic shadow or the electrical axis is compatible with the diagnosis

Diagnosis is favored further by the signs indicating the tugging of the heart on neighboring organs to which it is stuck These signs include the rib retraction described by Broadbent[16] and the jerking of the diaphragm demonstrated by x ray The sign called diastolic rebound is a phenomenon associated with systolic retraction of ribs and probably representing the diastolic phase of a to and fro movement of the chest wall Many more fancy signs such as Friedreich's[34] diastolic collapse of veins depend upon too many variables to permit the attachment to them of much significance in the diagnosis of mediastinopericarditis from other forms of chronic cardiac disease

Most patients with this type of pericardial disease run a course not very different from other patients with chronic rheumatic heart disease of comparable degree They may develop heart failure eventually which has the characteristics of congestive heart failure in chronic rheumatic heart disease Not enough work has been done but it appears probable that these patients with this type of pericardial fibrosis do not have inflow stasis until they develop the back pressure of myocardial failure Therefore the important interference of mediastinopericarditis is with systole not with diastole it is an obstacle to contraction not to dilatation This is as true as most generalizations about disease mechanisms we shall see that it is probable that cases exist in which both types of mechanical disturbance are present

tunity for successful treatment The varieties are (1) mediastinopericarditis and (2) constrictive pericarditis

Mediastinopericarditis

Mediastinopericarditis is for present purposes defined as fibrous pericarditis in which the fibrous tissue joins the heart firmly to adjacent structures the ribs and sternum the pleuræ the diaphragm and the structures behind the heart It is conceived on the basis of anatomical studies and certain physical signs that these firm attachments interfere with the contraction of the heart and therefore impose a burden upon it This burden is considered to be brought about by the necessity of pulling on these adjacent structures against resistance with each contraction of the heart This load is thought to be a factor in the cardiac enlargement exhibited by these patients and in the heart failure which many of them ultimately develop

Mediastinopericarditis is a rare condition discussed here mainly for contrast with the more frequent and important constrictive type In the sense that the term is used here mediastinopericarditis usually comes about as a late result of rheumatic fever It is found commonly therefore in association with rheumatic valvular disease This fact imposes great difficulties both on understanding the mechanical difficulties of the heart and on recognizing the condition in patients It is difficult or impossible to separate many of the effects of endocardial and myocardial disease on the one hand from those of pericardial disease on the other The evidence that an important degree of increased work is demanded of the heart by such adhesions as these is obtained at the autopsy table There is a general notion that the largest hearts are found in association with mediastinopericarditis but since these patients also suffer from valvular disease often multiple it is difficult to know how to assign credit for the hypertrophy Better evidence is to be found in such tabulations as those of Laws and Levine[47] As is shown in the accompanying table Table I taken from the paper of Laws and Levine[47] by permission of these authors the average heart weight of patients exhibiting mediastinopericarditis plus valvular disease is greater than in the patients exhibiting only valvular disease of similar variety and degree This suggests the probability that these external adhesions increase the work of the heart This probability is strengthened by the existence of certain physical signs soon to be mentioned

The recognition of mediastinopericarditis is difficult and dogmatic statements about individual patients rarely are justified Its presence is

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Constrictive Pericarditis

Constrictive pericarditis is defined as fibrous pericarditis in which the fibrous tissue forms a tight sheath around the heart in such a way as to interfere with its dilatation and limit its capacity The obstruction to the entrance of blood inflow stasis and the limitation to the capacity of the ventricles bring about a series of alterations in the movements of

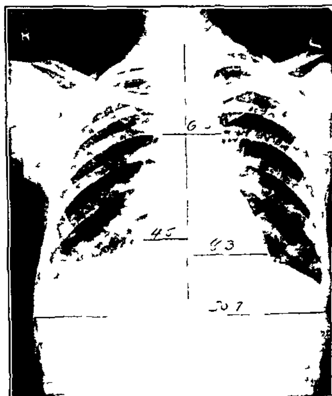


Fig 7 Anteroposterior film of patient with constrictive pericarditis The cardiac silhouette shows the absence of enlargement the sharp straight border and the loss of landmarks

the heart and the circulation and distribution of the blood which has been outlined on previous pages These alterations are highly characteristic and bring about an equally characteristic set of symptoms and physical signs *By some this is called Pick s disease or syndrome* constrictive pericarditis is a preferable term

There is no pathognomonic sign of constrictive pericarditis if indeed there is of any condition but there is a very significant and somewhat curious combination of signs The peripheral veins are engorged

and firm the liver is enlarged but *not* pulsating recurrent ascites frequently is the presenting symptom pleural effusion and dependent edema are not unusual Pulmonary congestion is less marked than peripheral and dyspnea at rest usually is not seen except when pleural effusion or ascites are of high degree The heart surprisingly in view of the congestion is not much if any enlarged Often its pulsations are neither seen nor felt the sounds are distant and murmurs absent Occasionally a third sound is mistaken for a diastolic murmur The pulse is small and paradoxical the arterial pressure low the rhythm most often regular although auricular fibrillation may be found Under the fluoroscope the excursions of the heart are reduced or even invisible especially over the right ventricle the shape of the heart fails to change with the phases of respiration the shadow of the superior cava may be widened and calcification is seen occasionally The electrocardiogram usually shows small complexes and flat T waves The significant center of this picture is the combination of a high degree of venous congestion chiefly peripheral with a normal sized or only moderately enlarged heart which is singularly quiet

There is another general characteristic of interest and diagnostic value Since the chief obstruction to inflow and filling is a morphological one not affected by rest or drugs the congestion is as it were a permanent one The venous pressure fluctuates a little with the removal of fluid from chest and abdomen but it remains high The congestion is no spring freshet running over the streams banks and no temporary backing up from the pump it is a valid and permanent dam

This type of fibrous pericarditis is in the writer s experience not the result of rheumatic fever It is frequently the sequel to tuberculosis of the pericardium of 25 successive cases tuberculosis was demonstrated in 14 occasionally it is caused by the pneumococcus or the staphylococcus albus sometimes there is neither organism nor characteristic lesion to identify the invader

It is an important disease to recognize because as we shall see when we come to discuss treatment skillful surgery can more often than not restore these patients to comfort and earning capacity The diagnosis must be thought of and the condition separated from its best imitators right ventricular failure due to heart or lung disease tricuspid stenosis and cirrhosis of the liver

Calcification of the Pericardium

Rather rarely and under circumstances not clearly formulated calcium salts may be laid down in the area of the pericardium These deposits

may occur as isolated islands thickly or thinly scattered flakes streaks or as a wall of rock around part of the heart s circumference Such calcification appears more commonly in old than in young people and the deposits usually are on the site of previously active infections They certainly appear in old tuberculous lesions and probably in some other varieties also Like the acute changes of inflammation they extend into and involve the myocardium It is necessary in such a general consideration as this one, to make only a few points about calcification of the pericardium

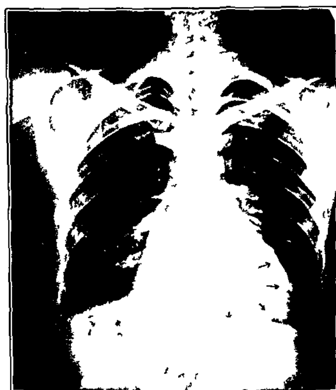


FIG 8 Anteroposterior film of patient with constrictive pericarditis with calcification *A rim of calcium may be seen along the left border* This is one of *the occasional* patients with an obstructing pericardium in whom the total heart shadow is enlarged

First the indispensable method of examination is by means of the x ray (Fig 8) From an extensive knowledge of the evolution of the situation in a given patient the presence of calcium may be suspected but not determined with any satisfactory degree of certainty save by the x ray

Second calcification of the pericardium may or may not be associated with important obstruction to the flow of blood Calcification is encoun

tered at operation in patients who present the picture of constrictive pericarditis it is also found sometimes in high degree in patients who suffer no real inconvenience from it On this account the presence of demonstrable calcification is not a clear indication of the need of treatment the decision as to this need is made on the basis of interference with the essential functions of the heart

Third calcification in the periphery of the heart is not always associated with disease of the pericardium A shell of x ray-opaque calcium containing material may be laid down as a late result of myocardial infarction streaks may represent deposits along coronary arteries calcification around diseased valves may extend to the outer surface of the heart or calcified deposits may occur in mural thrombi most often found in the left auricle

The recognition of this type of pericardial lesion by the x ray was foreseen by Diemer in 1899[7] According to Youmans and Merrill[m] the first case actually identified during life was described by Schwartz in 1910 Since then many cases have been reported It is worth while to look at the cardiac silhouette from many angles

The Causes of Disease of the Pericardium

The pericardium shares in the reaction of the body to a variety of disease producing influences As in dealing with the general problem of the etiology of disease these influences may be discussed under the following headings (a) congenital defect (b) trauma (c) poisons (d) deficiencies (e) infections (f) neoplasms (g) other and unknown disease producing influences

Treatment of patients with pericardial disease consists almost entirely of two types of activity (1) measures directed to the control or cure of the causes of the pericardial disease and (2) measures directed to the relief of tamponade

To avoid unnecessary repetition consideration of the management of tamponade will be reserved for a concluding section while the problem of treatment as it concerns etiology will be discussed in relation to each etiological category Of course in some forms of pericardial disease the same treatment may combat both tamponade and its cause The treatment of some of the etiological factors is dealt with in other chapters of The Oxford Medicine and consequently is not discussed in this chapter in these instances we shall deal in this chapter chiefly with certain specific problems of treatment related particularly to disease of the pericardium

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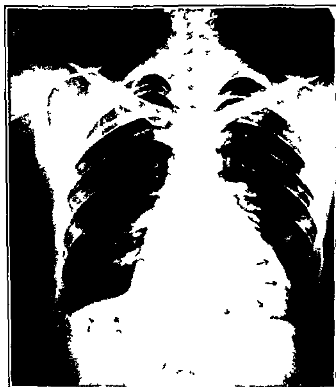


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feeble pulse hypotension weakness The most valuable signs in distinguishing one from the other is the degree of fulness of the veins or the height of the venous pressure the presence of a paradoxical pulse points to tamponade It is perfectly possible of course for both the loss of blood and its accumulation under pressure in the pericardium to have a part in the production of the symptoms

As we shall have occasion to see when the discussion on *Treatment* is reached paracentesis of the pericardium may result in injury to the heart or its coronary vessels and so to the development of tamponade Contusions usually do not give rise to tamponade but Dustin[30] has reported an interesting instance in which a contusion in a patient with the coagulation defect of hemophilia was followed by the development of hemopericardium

The prompt recognition of tamponade due to trauma to the heart and the assessment of its relative significance in a given case are important in *outlining treatment* Usually *this diagnosis is to be made on the basis* of the history and the physical signs The x ray and the electrocardiogram *may have evidence to contribute but this evidence is in such a* critical state as this may be sometimes not worth the loss of even a few *minutes of time from commencing operation necessary to carry them* out and see their results

The selection and carrying out of appropriate treatment in these cases may be life saving Because it is life saving requires great skill and deals *with an organ regarded as peculiarly vital the modern surgery* of the heart is rightly considered to be a great achievement No part of *this surgery is more definite or dramatic than the repair of bleeding* puncture wounds which have led to tamponade or hemorrhage which *threatens life*

The treatment of such tamponade is prompt operation This permits the *surgeon to relieve the tamponade by removing the blood in the peri*cardium and often to repair the leak in heart or great vessels which has led *to the tamponade A considerable number of cases have been re*corded in which wounds from knives or bullets have been repaired and a dying *patient restored to lasting health Bigger*[7] collected 53 examples of repair of heart wounds between 19 6 and 193 with 73 5 per cent recovery *He observes that pericardial wounds do not require surgery unless there is* hemorrhage or infection

The repair is the *vital therapy in this form of* hemopericardium If there has been much hemorrhage transfusion may be necessary However as Blalock has suggested[3] *transfusion* is not often effective if tamponade is marked since the injected blood remains trapped in the

Congenital Defect

Congenital defect of the pericardium has received some attention in the section dealing with changes in structure of the pericardium. Here there need only be added a brief note as to the mode of formation of the most common developmental anomaly. Keith[44] observes that the deficiency is on the left side of the pericardium and that in these cases the mediastinal aspect of the left lung lies directly on the heart; the phrenic nerve he found to descend quite close to the internal mammary artery. On the basis of his study of a group of malformed fetuses he concluded: *It was evident that the condition of the parts* had been produced by the lung bud growing within and expanding the communication between the pericardium and pleura, for that communication lies immediately central to the point at which the lung bud appears. The condition should be described as dilatation of the pleuropericardial foramen. As has been said, no effective means are at hand by which these defects can be recognized. Fortunately they require no treatment.

Trauma

Affections of the pericardium due to trauma are of considerable importance, partly because they are not particularly rare in combat with penetrating weapons, and partly because occasionally a situation arises in which appropriate knowledge may lead to recognition and effective treatment. Penetrating stab or bullet wounds are the more frequent source of traumatic injury to the pericardium, but as Warburg[65] and Bright and Beck[15] have shown recently, non penetrating wounds occasionally may cause *contusion* of the heart. *Rupture* of the pericardium may occur, usually as part of an extensive crushing injury (Crynes and Hunter[illegible]). Of these traumatic affections, penetrating wounds, contusions and rupture, penetrating wounds are much the most significant.

As a rule the result of a penetrating wound of the pericardium is puncture of the heart also. The blood lost from the cardiac puncture may be held in the pericardium. In this case the actual loss of blood probably will not be great, but as the intrapericardial pressure rises the signs and hazards of tamponade appear. If the blood lost through the cardiac wound is not retained by the pericardium but escapes to some adjacent freedom such as the pleural cavity, then the loss of blood may be greater, and the signs and dangers of hemorrhage develop. Tamponade and shock from hemorrhage have some findings in common: tachycardia

Deficiencies

Deficiency of specific substances is known to be a cause of pericardial disease As knowledge of this field is changing rapidly it is probable that what is said here soon will be subject to changes or additions It has long been considered that scurvy is a cause of pericardial effusion and known that this effusion usually is bloody In Hirsch s Handbook of Historical and Geographical Pathology [41] there is a description of actual epidemics of this manifestation of deficient diet In a Siberian prison camp in 1917 Hilt and Brull[10] saw among 6 300 men several hundred cases of hemopericardium probably associated with scurvy Of course similar bloody effusions may occur in pleural and peritoneal cavities also This type of pericarditis is a manifestation of the severer type of scorbutus The treatment of such hemopericardium is the administration of vitamin C The blood usually will be absorbed a few of the cases among war prisoners had a paracentesis because of a degree of tamponade considered to be dangerous

Now the utility if any of a classification of etiological factors such as this article follows is that it supplies a framework into which to fit a number of items in some sort of reasonable order The next group of causative factors are not deficiencies as these ordinarily are conceived but they are deficiencies in a wider sense It is now proposed to consider the pericardial reactions brought about by deficiency of proteins in the blood of thyroid secretion in myxedema and of oxygen and other essentials in myocardial infarction

The first of these is dismissed easily Patients with severe *hypoproteinemia* may suffer from pericardial effusion usually in association with accumulation of fluid in other parts of the body This fluid is low in cells and in protein it seldom produces an important degree of tamponade The treatment is the restoration if possible of normal protein levels in the blood

Gordon[26] and others have described interesting examples of the occurrence of pericardial effusion in *myxedema* These are non inflammatory accumulations which may reach great size in Gordon s case 1 600 c c were removed at one tapping and in Freeman s 1 400[3] This may bring about severe symptoms of disorder of the circulation It is even suggested that an unrecognized pericardial effusion frequently may be a significant factor in the so called myxedema heart No friction rub is present the administration of thyroid is followed by elevation of the metabolic rate and resorption of the fluid The latter may take place with very considerable rapidity

venous system by the obstruction to inflow to the heart. In the case he described a transfusion failed to alter the arterial pressure but raised the already high venous pressure. When the tamponade was relieved by operation the venous pressure fell and the arterial pressure rose.

Little is known about the treatment of contusions; presumably they should be managed on the principles that govern the care of a patient with myocardial infarction.

Poisons

Poisons rarely operate as causes of reaction on the part of the pericardium. It is true that Dakin's solution has been introduced by Beck and Griswold[8] into the pericardial cavity of animals and this introduction has been followed by exudation and eventually by fibrosis. Blalock[9] has produced various types of pericarditis by the introduction of aleuronat into the pericardium, and other workers have used a number of substances in a similar way.

There is little evidence that such a mechanism operates in the production of disease in man. It has been suggested more than once that the *pericarditis of uremia* is caused by some toxic substance retained in the body as a result of renal failure. Actually the cause of this form of pericarditis is not known. There is usually a fibrinous exudate, but it is a sterile one as a rule, and so far no chemical substance has been found guilty of producing the reaction.

Patients with uremic pericarditis usually are patients with progressive disease of small arteries, and it is possible that so-called "uremic pericarditis" is a manifestation of local vascular degeneration. The difficulty about this explanation is the fact that it occurs usually in association with unquestioned renal insufficiency and not merely with progressive vascular disease. Moreover, it is often a terminal event and as such may be part of a general breakdown in which there are many factors rather than a single dominant one.

However produced, this form of pericarditis usually manifests itself by a friction rub. Extensive accumulation of fluid is rare. The chief importance of making the diagnosis is that it is of some value in prognosis. The great majority of patients with uremia and pericarditis will die shortly, but there are enough exceptions to make this less than an absolute rule. Uremic pericarditis plays such a small part, if any at all, in the patient's disability that it requires no treatment. The renal insufficiency and its cause are the problems to attack with such therapeutic measures as are available.

Rheumatic Pericarditis

In parts of the world where rheumatic fever is frequent a reference to pericarditis ordinarily means the type associated with rheumatic fever. This type usually occurs in association with other evidences of rheumatic injury to the heart. It may be limited to a small area of fibrinous exudate; there may be such an intense exudation that the surface of the heart is shaggy with matted strands, or a serofibrinous effusion may develop. Usually rheumatic inflammation of the pericardium heals effectively, so effectively in fact that Massie and Levine[61] have emphasized the relatively good outlook of patients whose sole or chief rheumatic manifestation is pericarditis. Even if the acute pericarditis is very severe the patient, if he escapes valvular disease, may recover so that he shows no evidence of heart disease. In a few cases, almost always in patients who also have valve disease, the acute phase of pericardial inflammation is succeeded by healing with the formation of fibrous adhesions. Such scarring may result in merely a thickening of one layer of pericardium; it may join together the more or less thickened layers, or it may bind heart and mediastinum into the union called mediastinopericarditis. About the only thing it does not do, so far as present evidence goes, is to produce the striking picture already described as constrictive pericarditis.

Perhaps the recent work of Drinker and Field[79] throws some light on why rheumatic pericarditis may be followed by restoration to an essentially normal state or by these various degrees of scarring. They found that a high content of protein in intercellular fluid seemed to encourage the growth of fibroblasts. It is true that pericardial transudates which are low in protein are not followed by fibrosis, and it is true that exudates, e.g. those due to rheumatic fever or tuberculosis, which may be high in protein, may be followed by extensive adhesions.

In patients dying with active rheumatic fever pericarditis is a lesion observed frequently. In the 74 cases of fatal acute rheumatic fever observed at autopsy by Bland and Jones[7] 55 per cent showed evidence of acute pericarditis and 80 per cent showed evidence of some form of pericardial involvement. This involvement, however, rarely was important as a cause of death. When fluid was present usually there was less than 200 c.c. but in a few cases amounts up to 1 200 c.c. were encountered.

When fibrinous pericarditis only is present it shows itself by a friction rub as has been described. When effusions occur they usually accumulate slowly enough for the sac to stretch so that the increase in intra

Cardiac infarction based upon coronary obstruction is a frequent cause of pericarditis Severe deficiency in local blood supply leads to necrosis if the necrotic area includes or approaches the pericardium as it often does a pericardial reaction follows

The reaction is characteristically a fibrinous exudate it may end up as a patch of fibrous thickening Cases are on record such as the one reported by Master and Jaffe[52] in which pericardial effusion has followed coronary obstruction The usual reaction is one that leads to a friction rub which most often becomes audible on the second or third day of illness It is rarely loud usually transient and often variable Rarely it lasts or recurs for weeks but the one patient under my observation in whose case this was observed probably had a series of myocardial infarctions rather than a single one The appearance of a pericardial friction rub may be a sign helpful in the diagnosis of coronary occlusion and it should be sought with care as good evidence of infarction but having been found it requires no direct treatment although it may influence the general management of the patient According to Levine s extensive statistics[45] such a friction rub occurs in about 15 per cent of patients with acute coronary occlusion it appears to have no prognostic implications as to the course of the patient s illness

Infections

Infections certainly are the most frequent and important proximate causes of pericardial disease A large number of infectious agents are known to play this rôle including *Bacillus tuberculosis Streptococcus hemolyticus Staphylococcus aureus Pneumococcus* the etiological agent whatever it is causing rheumatic fever and less frequently *Meningococcus Gonococcus Bacillus tularense* or *Actinomyces* Pericarditis may occur in measles and in smallpox Syphilis is infrequent as a cause of pericardial disease although occasionally a pericardial reaction may be demonstrated on the surface of a syphilitic lesion of the heart Infections apparently gain access to the pericardial cavity by the blood stream by lymphatics or by extension This extension may take place from abscesses in the heart muscle from lymph glands lying outside the pericardium from adjacent pleural cavities or from other nearby organs Sometimes of course infection is introduced from without in the course of traumatic injury

The types of pericarditis associated with rheumatic fever with tuberculosis and with pyogenic infection may be selected for special description at this point

culosis of the lymphatic system or of pleura or peritoneum it is relatively unusual to see it in association with active pulmonary tuberculosis of the chronic ulcerative variety It may occur as part of a generalized miliary infection It appears that most cases are brought about by an extension of an adjacent infection to the pericardium This frequently comes from caseous mediastinal or peribronchial lymph glands which occasionally even rupture into the pericardial cavity Extension may take place also from pleura or lung It is more frequent in men than in women and appears more often in patients over 40 years of age than do other forms of serous membrane tuberculosis

During its often long and wasting course tuberculosis of the pericardium may produce several morphological varieties of pericarditis Early in the course there may be only the manifestation of fibrinous pericarditis fever rapid pulse a friction rub and perhaps pain without any characteristic pointing to a tuberculous etiology It is assumed but hard to prove that in some such cases the pericarditis follows a self limited course as do many cases of tuberculous pleurisy and heals without important permanent damage It is more often the result that the fibrinous exudate is succeeded by a slowly accumulating effusion Probably even this process may reverse itself in a few fortunate patients the fluid disappears and with it the signs of tamponade Usually however although the fluid diminishes in volume and the shadow of the heart pericardium complex grows less the signs of obstruction persist. In this case the activity of the disease process has continued and pericarditis with an obstructing effusion has been succeeded by pericarditis with an obstructing scar This situation may cease to be visibly progressive and the patient present an example of chronic constrictive pericarditis in which signs of infection are slight or absent and the disability is due to mechanical obstruction to the filling of the heart. These patients with a high degree of obstruction a small quiet heart and a slow progression are on the whole those in whom the tuberculous infection tends to heal by fibrosis There are others in whom this tendency is less vigorous the tuberculous fire continues to burn the signs of active infection accompany those of tamponade and the course is rapidly downward At autopsy these patients hearts often are embedded in a mass of tissue replacing the pericardium (Fig 2) there are areas of caseation and collections of pus in abscess-like cavities There may be similar activity in the adjacent mediastinum and I have once seen this sort of process involving a large share of the pleura

The prognosis of recognizable tuberculous pericarditis is grave but probably not as gloomy as many series of cases indicate The difficulty

pericardial pressure may not rise to heights which produce dangerous tamponade Large effusions always produce some tamponade however and its degree may increase with some suddenness, so that vigilance is desirable With a given amount of fluid of course the pressure is greater on the way up i e when it is accumulating than on the way down, i e when it is being resorbed

The diagnostic problems in rheumatic pericarditis are many but the important ones are two (1) Is the pericarditis rheumatic? and (2) Is the picture due to pericardial effusion or to dilatation with failure?

The first question usually is answered by the associated evidence of rheumatic activity one rarely is justified in seeking an answer to it by pericardial paracentesis unless there is some reasonable possibility of purulent pericarditis

The second question often is difficult to answer because the two conditions have many manifestations in common enlarged dulness and shadow tachycardia and peripheral congestion A paradoxical pulse points to tamponade and a gallop rhythm to failure The sounds and the pulsation usually are much more damped in fluid than in failure and even a very large heart fails to produce a Ewart s sign

When rheumatic fever involves the pericardium it still presents the problem of the treatment of the rheumatic fever process The rest in bed the drugs the nursing care and the food which are recommended in the case of other manifestations are to be used here Salicylates do not appear to influence the course of rheumatic pericarditis Pain may be severe enough to suggest sedatives The factors that determine the amount of exudation and the rapidity of reabsorption in rheumatic pericarditis are not well understood In most patients the fluid is not great enough in amount or rapid enough in accumulation to obstruct the circulation to a dangerous degree but it may do so and this problem will be discussed when we come to the treatment of tamponade as such

Tuberculous Pericarditis

In some clinics rheumatic fever is the leading cause of pericarditis in others tuberculosis plays this rôle Between them the two probably account for the majority of cases Of the two tuberculous pericarditis is longer more severe more varied in course and much more dangerous There has been a recent awakening of interest in it attested by several excellent reports including those of Harvey and Whitehill[37] Blalock and Levy[11] and Keefer[43]

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The prognosis of recognizable tuberculous pericarditis is grave but probably not as gloomy as many series of cases indicate The difficulty

in making a good estimate of the relation of deaths to recoveries lies in the fact that it is usually only the patients who have had a paracentesis a decortication or an autopsy in whom the diagnosis can be made with certainty

The signs and symptoms of tuberculosis of the pericardium include those of the infection and those of the pericardial reaction Fever is the rule but may be absent leucocytosis and anemia are seldom of impressive degree The local signs may be those of fibrinous pericarditis effusion often recurrent or constriction When pleural effusion is present it may be the result of tamponade of tuberculous pleuritis or of a combination of the two In the last case one may find a fluid of low specific gravity but containing enough tubercle bacilli to kill a guinea pig

Keefer divides cases of tuberculosis of the pericardium into five groups as follows

(1) Patients with symptoms and signs of a wasting disease and obscure fever
(2) Patients with symptoms and signs suggesting heart failure with congestion
(3) Patients with symptoms and signs of multiple serous membrane tuberculosis
(4) Patients with symptoms and signs of a massive pericardial effusion
(5) Patients with symptoms and signs of miliary tuberculosis

In the writer s experience the conditions with which pericardial tuberculosis is confused most often include chronic heart failure based on coronary disease hepatic cirrhosis other forms of acute pericarditis especially rheumatic pericarditis and although less often purulent pericarditis

Tuberculous pericarditis presents a particularly important and difficult problem in therapy It is a prolonged dangerous business apt to go on much longer than tuberculous activity in pleura or peritoneum and with a much greater threat to life than either Death results from progression and extension of the infection from tamponade or from a combination of the two The measures used to combat the infection do not differ from those used in other kinds of tuberculosis except that they are less effective The removal of fluid by paracentesis and the excision of parts of the diseased pericardium do not demonstrably influence the course of the infection for better or for worse Their function is the relief of tamponade this will be considered presently

Several workers beginning with Emile Weile and Loiseleur [1] or with Wenckebach[66] in 1910 have tried to influence the course of tuberculous

pericarditis by injecting air into the pericardial cavity Sometimes the paracentesis relieves some of the patient s symptoms but it is difficult to find evidence that the air has done more than facilitate the production of some interesting x ray plates

This is to say that no effective local treatment for tuberculous pericarditis has been devised

Purulent Pericarditis

Infection of the pericardium with pyogenic organisms occurs most frequently in severe cases of pneumococcus pneumonia in infections with staphylococcus aureus such as osteomyelitis and in the cases with penetrating wounds It may occur also in other infections It is a severe disease which may be fatal unless recognized and treated in time and which progresses sometimes with startling rapidity In many instances there is a perfectly obvious septic process as a source for the spread or transport to the pericardium in others the purulent pericarditis may dominate the picture and the original infection may be forgotten or apparently insignificant

The general manifestations are those of infection usually with appropriate reflections in temperature leucocyte count and degree of prostration The local manifestations are those of fluid in the pericardium including cardiac tamponade of a severity often apparently out of proportion to the amount of fluid present Presumably this disproportion is based on two characteristics of pyo pericardium the amount of fluid may increase with great rapidity and the pericardium under these conditions of inflammation may have less capacity to stretch At operation one may see only a few hundred cubic centimeters of pus which have produced really threatening tamponade because the sac is thickened and not easily distensible

The main factor in the diagnosis of purulent pericarditis is thinking of it as a possibility the same may be said of the tuberculous variety Friction rub is more often absent than present and the amount of fluid usually is not great enough to give an extreme picture of effusion The essential point is the combination of tamponade and acute infection This is one situation in which paracentesis pericardii or pericardiostomy may be used justifiably for diagnostic purposes a point to be discussed more extensively shortly

When purulent pericarditis has been demonstrated and found to be due to the pneumococcus streptococcus staphylococcus or others of equal pyogenic vigor the treatment is prompt surgical drainage This

necessity is not based on the severity of the tamponade but on the presence of pus in the pericardial cavity nevertheless tamponade often is severe in these cases and relief correspondingly great So far as we now know serums and drugs specific for these organisms while they may well be used should be used as additions to and not as substitutes for the establishment of surgical drainage

Neoplasms

Neoplasms are relatively infrequent invaders of the pericardium Primary growths are particularly rare but Yater[69] in an extensive search of the literature has found records of a few, mostly sarcoma or lipoma Metastases from primary growths elsewhere occur occasionally in the pericardium Heninger[18] has described a series of cases illustrating some of the less unusual associations These include examples of epithelioma extending from the pleura hypernephroma invading the pericardium via the heart esophageal carcinoma involving pericardium and mediastinal glands and carcinoma of the lung with extension to the adjacent pericardium

Effusion occurs in many such cases both primary and metastatic The fluid often is bloody and may contain identifiable tumor cells The x ray may show the fluid and may sometimes contribute the evidence of localized irregularity of the heart pericardium shadow Boman s[13] patient with primary sarcoma had pain radiating to the right shoulder This patient s electrocardiogram exhibited inverted T_2 and T_3 a friction rub was heard over the precordium

The diagnosis of tumor is uncertain unless there are tumor cells in the fluid or a fairly obvious source of metastasis The only patient in whom the writer has ventured the diagnosis in the absence of these cardinal pieces of evidence has been in a stationary condition for several years and probably has healed pericardial tuberculosis

Other and Unknown

Pericardial reactions occur in some other conditions besides those mentioned Effusion is observed in some cases of periarteritis nodosa or disseminated lupus erythematosus It is found also and may be important in patients with the edema of heart failure or of nephritis In all of these instances the signs are those of effusion the diagnosis is particularly difficult in the patients with congestive heart failure (compare the section on rheumatic pericarditis)

The Treatment of Patients with Pericardial Disease

The management of patients with pericardial disease resolves itself into three major activities

(1) The care of the patient

(2) The treatment of the factors leading to pericardial disease

(3) The treatment of tamponade and other disturbances of function resulting from pericardial disease

The care of the patient may be mentioned because in a collection of chapters severally devoted to specific organs the total organism is in some danger of being lost to sight The management of the underlying factors has been considered in the section dealing with etiology We turn now to a discussion of the treatment of tamponade and other disabling disturbances of function resulting from pericardial disease

The Treatment of Tamponade

Tamponade may be due as has been said to liquid or gas in the pericardium or to constricting scar The problem of its treatment therefore arises frequently This problem has been considered already as it concerns the special difficulties of traumatic hemopericardium it is now to be considered in relation to pericardial fluid from other causes Tamponade due to fluid may be relieved by the gradual progress of reabsorption or more rapidly by paracentesis or incision Most effusions due to inflammation run a self limited course and do not require direct removal It may be said generally that there are two important situations which indicate a need for direct action (1) tamponade which is progressing to a point where life is threatened (2) the necessity of positive information as to whether the fluid is purulent or not

In the absence of one of these indications usually it is well to avoid paracentesis and even these guides must be followed with caution Paracentesis pericardii is an operation of respectable antiquity Riolanus is said to have suggested it in the 17th century However there has never been agreement as to a satisfactory method for carrying it out It is difficult to be sure at all times of just where the point of the needle is The larger the amount of fluid in the pericardium the safer is its puncture thus the method is better for treatment than for diagnosis

The dangers of paracentesis are several

(1) The heart may be entered by the needle This is not necessarily harmful as any one knows who has taken blood from dogs or rabbits by cardiac puncture but if the heart wall is thin as in the auricle or if it is

weakened by disease as it may be in tuberculous pericarditis then even a neat puncture may be followed by hemopericardium and increasing tamponade

(2) A coronary artery may be injured Levine[19] has seen two such cases with resulting slow leakage of blood into the pericardial cavity

(3) The internal mammary artery may be injured

(4) It is possible to carry infection into the pleural cavity or even the peritoneum

One might expect to encounter pericardial "shock as an analogue of pleural shock It is referred to occasionally but not very impressively and if it occurs at all must be extremely rare

These dangers exist and one may find in many writings[37, 57] reports of catastrophes or near catastrophes associated with paracentesis The existence of danger does not mean that the method is to be given up but it does mean that the dangers ought to be minimized by wise selection of cases and of method and balanced carefully against the possible benefits of the procedure It has been said that the larger the effusion the safer the puncture thus the treatment of large effusions by paracentesis is seldom dangerous unless the diagnosis is wrong

Before considering the technique of paracentesis we may scrutinize the two major indications for it Dangerous tamponade is not a frequent phenomenon in pericarditis with serous effusion In most patients rheumatic tuberculous or with heart failure the sac stretches enough to keep the pressure within limits endurable by the body However dangerous tamponade may occur and patients may die of it

It is to be remembered that peripheral edema in pericardial disease usually is associated with long standing tamponade rather than with rapidly increasing tamponade It is the latter that may although certainly not often threaten life Williamson and I ts[68] have described the autopsies of four patients who died of advancing tamponade Such patients commonly exhibit a rising venous pressure and a falling arterial pre sure The latter measurement is the one most readily followed if it falls progressively and particularly if there is a sudden increase in the rate of fall then relief may be necessary Such progression occurs most frequently in rapidly accumulating effusion and rapidity of accumulation occurs in about this order hemopericardium first pyopericardium second non purulent exudates third and transudates fourth

The treatment of hemopericardium by operation has been considered already as has that of pyopericardium The transudates of heart failure nephritis and nutritional edema rarely lead to dangerous degrees of obstruction and they respond to diuretics and to the measures directed

at the underlying disturbance so that pericardial puncture is rarely indicated in this group It follows that the problem of progressive tamponade if we exclude the bleeding patients and those with pus is most frequent in patients with rheumatic or tuberculous pericarditis and met with occasionally in other kinds In any of these varieties the physician occasionally may be convinced that failing to relieve the tamponade is more perilous than relieving it In this situation a further decision must be made is the tamponade to be relieved with a needle or by operation and incision? The latter may be done quickly and easily (see Cutler and Beck [4]) and under some conditions apparently is safer than the insertion of a needle Sir Charles Ballance observed in 1920[3] The operation of paracentesis pericardii or aspiration of the pericardium should be I think banished from surgical practice just as puncture of the distended intestine is no longer done in cases of obstruction It is a leap in the dark and many cases of wound of the heart or coronary artery have occurred in the course of this operation This seems a little extreme there are cases of very large effusion or recurring effusions when paracentesis may have clear advantages over operation Circumstances must decide in each instance which method is to be adopted

Exploration of the pericardium may be indicated also by the need of positive knowledge of the nature of the fluid This usually means the need of knowing whether or not it is purulent If there is doubt about the presence of fluid and about its nature and if it may be purulent then in my opinion exploration by operation is preferable to exploration by puncture

When the decision to enter the pericardial cavity has been made and when exploratory incision by a surgeon has been rejected in favor of puncture by needle the problem of the point of attack arises No fixed policy no ideal route exists A large effusion presumably non purulent may be wisely approached via the fifth interspace near the outer edge of the area of dulness Sometimes the dulness extends laterally beyond the apex impulse and in this circumstance it is probably best to enter this outer zone This approach is ordinarily used in the occasional patient who has recurrent effusion with disabling tamponade

Conner [1] in the case of large effusion with physical signs over the *left back* has found it useful to *drain the pericardium through a needle* inserted into the left back guided by the area of flatness White[67] reports withdrawing 500 c c of pericardial fluid by this method after several attempts by way of the anterior chest had failed to strike oil One wishes to be quite sure of two points before using this route first that the signs

in the back really indicate a large pericardial effusion, and second, that the fluid is not purulent

The possibility of purulent fluid makes an extrapleural approach desirable A useful consideration of paracentesis pericardii is quoted here from Homans[4] Aspiration of the pericardium exposes the patient to the risk of injury to the heart which even in the presence of a large effusion must lie in contact with the anterior thoracic wall In fact aspiration in the anterior area left uncovered by pleura is too dangerous to contemplate for over and beyond the damage which the needle might do to the heart s muscle it may readily wound the exposed coronary artery as it passes down between the right and left ventricles According to Conner a considerable effusion pushes the lung against the lateral thoracic wall leaving areas both in front and behind where the two pleural surfaces are pressed together In either of these areas (1) to the left of and below the apex beat and (2) in the flat triangle mesial to the scapula rheumatic effusions which will not infect the pleural cavity can if necessary be tapped But for suspected purulent exudates the risk of transpleural aspiration would be too great The needle had better enter by Sauerbruch s route just to the left of the ensiform where it avoids the internal mammary artery but instead of passing sharply upward should be directed slightly upward and sharply backward to avoid the heart and enter the left lateral pouch of the dilated pericardium The needle should have a diameter of 1 mm or more according to the suspected quality of the fluid which should be withdrawn by the aid of suction

By whatever route performed paracentesis should be preceded by adequate local anesthesia By adequate is meant not only carrying the injection deep enough but allowing enough time to elapse for the drug to take effect Furthermore after any paracentesis of the pericardium the patient should be observed systematically for a period of hours in order to recognize the increasing tamponade which may come with bleeding from the heart The blood pressure the degree of venous distension and the character and intensity of the heart sounds should all be noted

Disabling pericardial obstruction may be due also to a constricting scar Constrictive scars are due as has been said usually to tuberculosis occasionally to infection with staphylococcus or pneumococcus and apparently never or hardly ever to rheumatic fever In many of these patients the disability and danger resulting from constriction are relieved by the so called Delorme[6] operation To carry this out a surgeon with expert knowledge of this special field of surgery is to be sought The essential operative procedure appears to be the removal of fibrous tissue from the surface of the ventricles often including part of the thickened

epicardium and the operation may be called a success if (1) the surgeon is able without mishap to excise enough of the scar to permit adequate filling of the heart (2) the heart muscle is able to carry this increased work and (3) the underlying disease does not continue to progress

Under what circumstances is this operation indicated? It may be accepted that when constriction is associated with a pyogenic infection the pericardial cavity should be drained and an appropriate amount of the thickened pericardium removed It may also be taken as accepted that when a patient exhibits the evidence of a disabling degree of constriction due to a healed inactive process whatever its etiology pericardiectomy is indicated Indeed in such a patient long delay is contraindicated since the longer operation is postponed the more chance there is of atrophy of the underworked heart muscle Such atrophy increases two dangers of the procedure that of entering the heart during the operation and that of dilatation and failure of the heart after its release

The patient who has constriction without activity has only a mechanical cause for his symptoms and may be relieved by mechanical means The patient who has both constriction and an active disease process has both as causes for his symptoms and the problem of treatment is accordingly more complex This problem arises in patients with chronic tuberculosis of the pericardium There is a widely held opinion that activity of the tuberculosis means that operation is apt to be ineffective and that it may act also to accelerate the progression of the infection Both these points are on the whole reasonable but my experience in both Tennessee and Massachusetts indicates that there are cases in which operation during the course of active infection has relieved the obstruction to the circulation and has not prevented the recession of the infection to apparent inactivity It may be noted that most of the patients studied by Burwell and Blalock[17] had activity in the sense of demonstrable tubercles in the portion of pericardium removed at operation the sort of activity in the presence of which operation is less effective is proliferative activity It is quite true that pericardiectomy in the presence of active proliferative tuberculosis is less effective and more difficult than when the process is healed or healing but there is no very impressive evidence that such an operation makes the infection worse although it is certain that tuberculous pericarditis may continue to progress after such an operation Therefore even in the face of proliferative activity operation may be practicable and the decision for or against it should be made on the basis of the *severity of interference with the circulation* rather than on the basis of the presence or absence of activity

When obstruction is the chief manifestation of the disease operation

is indicated when obstruction is relatively unimportant and infection the chief injurious factor a waiting policy is preferred When both obstruction and infection are important the decision is to be made on a careful balancing of the advantages and disadvantages of both courses On the whole when severe and injurious obstruction is present operation should not be withheld too long My own experience includes 9 patients operated upon for constrictive pericarditis at a time when the pericardial tuberculosis was grossly active Of these 2 died within 12 hours of the operation 2 died of miliary tuberculosis within six months of the operation and 5 are living all more than two years after the pericardiectomy Of the 5 4 are clearly improved one is still obstructed to about the same degree that he was before operation

We have been discussing the treatment of constrictive pericarditis by an operation which removes part of the scar and permits the ventricles more dilatation There are however cases of obstruction so mild as not to justify this procedure there are patients who need the operation but who for one or another reason do not have it and there are patients who although operated upon still have obstruction To meet these situations there are procedures which help to manage the symptoms although they do not cure An example is to be found in the life of Finsen[55] who suffered from constrictive pericarditis for some twenty years and who died only a year after the Nobel prize had recognized his contribution to knowledge of the use of light in the treatment of disease Finsen suffered particularly from recurrent ascites and in an effort to minimize the number of abdominal paracenteses he limited his fluid intake ate less salt and encouraged diuresis These methods are still useful and the development of mercurial diuretics which can be used repeatedly has provided a new and effective aid As in any patient with edema of mechanical origin it is worth while also to maintain a normal level of proteins in the blood

Digitalis is often given but usually is not effective probably because the congestion is due to mechanical obstruction rather than myocardial failure *There is some evidence that this drug occasionally may make the* situation even worse by slowing the heart rate and interfering with what appears to be a useful degree of tachycardia However no general prohibition is made and there are several circumstances under which the administration of digitalis to these patients is indicated (a) when patients with constrictive pericarditis also have auricular fibrillation and an over rapid rate (b) when patients with constrictive pericarditis also have myocardial failure probably a rather rare combination (c) as a preparation for pericardiectomy which may by releasing the atrophied

heart lead to its dilatation and failure in the face of unaccustomed demands

The Treatment of Mediastinopericarditis

It has been pointed out that mediastinopericarditis is an occasional sequel to acute rheumatic pericarditis When this occurs usually there are multiple causes of disability including valve disease and in the over work of the heart the external adhesions are only one factor In 1903 Brauer[14] suggested an operation for reducing the work of the heart in these cases It consists in the resection of several ribs and cartilages on the left side for some 10 to 15 cm from the sternum and it was expected to have its effect by removing the necessity of pulling in the ribs with each contraction of the ventricle There are a few examples in which the procedure appears to have been useful but in most cases it appears that the associated valve disease has been more important in causing the failure than the pericardial adhesion When myocardial failure not pericardial obstruction occurs in mediastinopericarditis it is best treated like heart failure associated with valvular disease or hyper tension

* * *

In conclusion one generalization about pericardial disease may be repeated the accurate description of a given example of pericardial disease in terms of etiology structural changes and changes in the func tion of organs usually will supply a basis for the planning of rational and frequently effective treatment Sometimes the treatment is directed toward the causative factor sometimes toward modifying structure or function It is therefore essential to have an understanding of each

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CHAPTER X

THE CIRCULATION IN INFECTIOUS AND TOXIC PROCESSES INCLUDING ACUTE ENDOCARDITIS

By Ivy Mackenzie

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INTRODUCTION

It is generally accepted as axiomatic that the heart may be affected in all acute infectious and toxic states. The terminal phase of every fatal process of acute poisoning is marked by abnormal rate and sometimes by abnormal rhythm of the heart's action, followed by gradual decline in the efficiency of the circulatory apparatus. But the term "cardiac failure" is employed in a loose and indefinite sense in these conditions: it is used without reference to other factors which may be determining the issue, and without recognition of the fact that, in the great majority of cases, the cardiac failure itself is but an expression of general organic dissolution. In the terminal phase of pneumonia, for example, every system of the body has been poisoned by specific toxins, by vicious products of abnormal metabolism, and by deprivation of a normal oxygen supply, and failure of the heart is usually not the cause but a sign of death.

In approaching a problem of this nature, it is necessary to consider as a preliminary step the contribution which pathological anatomy can offer to

its solution Is there any evidence that the disordered function of the circulatory apparatus has an explanation in structural degeneration? Does the cardiac muscle or extra cardiac system or the regulatory apparatus show anatomical evidence of disease which by itself may be reasonably held to account for circulatory failure? Is there anatomically speaking any distinguishing feature of the circulatory system which is peculiar to individual infections or intoxications and if so what are these features and to which specific diseases do each belong? An attempt will be made to answer these questions in the light of a short review of the main pathological changes of the most common infections and intoxications which are supposed to involve in their progress a disability of the organs in respect to blood supply

Of the greatest importance in dealing with this question, is a recognition of the fact that the heart is only one part of the circulatory apparatus It is of course the central and most highly specialized part and in this respect is peculiarly vulnerable to toxic influences Damage to its structure or interference with its regulation is incomparably more serious for the organism than any possible involvement of its auxiliary branches But it is the whole vascular system and not the heart alone which constitutes the organ of circulation and in many acute processes it is impossible to estimate clinically or anatomically the extent to which the central organ on the one hand or its arborization on the other is involved This is neither the time nor the place in which to discuss the part played by the peripheral circulation in maintaining an efficient blood supply It must be accepted as a fact that the function of arteries and veins is no mere passive one although the nature and conditions of their propulsive activity may be complicated and obscure It is sufficient for the present to emphasize the fact that patients who die with 'cardiac failure in acute infections succumb to toxic influences which affect the heart the peripheral circulation and regulating apparatus and not only these but in varying degrees the nervous and respiratory systems Assimilation and excretion may be perverted or diminished and the lungs kidneys brain or alimentary tract may in individual cases, constitute the main seat of reaction which determines the result

The cardiac rate is as a rule affected in the febrile conditions Physiologists state and it is consequently assumed that "the accelerated heart rate in fevers is due probably to the direct influence of the high temperature upon the heart itself For the clinician the matter is not quite so simple There are of course degrees of temperature which endanger life but for practical purposes fever is regarded as a sign of disease just like a rash or a cough and the feeling of fever of which the patient complains is a symptom just like palpitation or colic In some fevers for example in typhus and in pneumonia the pulse is rapid in others such as typhoid and epidemic

meningitis the pulse is relatively slow The pulse varies in fever not according to the temperature but according to the specific properties and affinities of the poisons which are generated directly or indirectly in the course of the infection Marris has found that the slow pulse of the febrile stage of typhoid is not accelerated by atropine thus distinguishing it from the pulse of many other diseased states and also from the pulse of healthy persons This discovery may or may not be of diagnostic importance but it is of the greatest significance as indicating the possibility of ascertaining facts regarding the toxic influence of infections on the regulatory apparatus of the circulation It suggests if not a method at least a point of view from which to approach the problem of post febrile cardiac irritability so often seen after influenza trench fever and occasionally after typhoid itself

The subject matter of our study is so comprehensive and the phenomena which it comprises so complicated that it is necessary to define in the first place the limits of the field of disease to be dealt with and in the second the method of survey to be employed The infectious and toxic processes of disease represent a large portion of the whole field of pathology The circulatory system is the vehicle of nutrition for the whole organism and in its functional activity it is delicately adjusted to the demands of the whole economy The efficiency of its activity may be prejudiced by damage involving its structure or by poisons which depress or exhaust its vitality without producing gross or even microscopic lesions On the other hand it may fail in its accommodation by virtue of the mechanical burden it is called upon to bear as for example in the bronchopneumonia of children with rickety chests and extensive atelectasis where it is deprived of the normal accessory forces of the respiratory movements

It is obvious then that an exhaustive treatment of the problem would carry us far beyond the object we have in view that object being the presentation of the main features of the subject which are of practical importance to the practitioner not only in recognizing pathological states and in providing a rational basis for treatment but in stimulating his interest to further observation beyond the confines of our present knowledge By infectious and toxic processes is meant here (1) the acute infections such as typhoid typhus scarlet measles whooping cough diphtheria pneumonia trench fever and the pyogenic infections (2) the subacute infections or granulomata syphilitic and tuberculous and (3) those infectious or toxic processes such as rheumatism chorea pernicious anemia and metallic poisoning in which reasonable doubt may be entertained as to the causal participation of organisms

The method of survey will include (1) a general review of the structural and functional disorders of the circulatory system which are characteristic of these infectious and toxic processes and (2) a special review of the

individual infectious and toxic processes in so far as their course is influenced by involvement of the organs of circulation

The General Pathology of the Circulation in Infectious and Toxic Processes

Pathological anatomy is the groundwork of modern medicine Other sciences make their indispensable contribution to the successful practice of the medical art but the conception of a structural basis for disease is the fundamental principle to which every other consideration must be subordinate In the classical work of the Hunters of Rokitansky and of Virchow the foundations of scientific medicine have been laid and to overlook their work and its developments is to venture into an atmosphere of chaotic and futile speculation

But the physician who expects from the pathological anatomist the explanation of all the complaints with which he has to deal is entertaining a vain hope Only a limited number of complaints can be correlated with the conventional designations of pathological nomenclature for complaints belong to the realm of mind while diseases fall into the sphere of biology in its narrower sense The problem is only partially relieved of its intricacy by setting aside the psychological element of the symptom or the peculiar individual coloring which each patient in virtue of temperament or disposition gives to his own account of his disability There remains for consideration the fact that the organism may suffer in one or more of its systems from the transient effects of poisons which possess a special affinity for special structures without producing results which come within the purview of the anatomist Alcohol morphin strychnin muscarin nicotin and pilocarpin may give rise to symptoms derangements or disabilities whose fleeting course leaves no trace of organic damage and whose interpretation even in the hands of physiologists or pharmacologists is more or less a matter of opinion The noxious substances elaborated directly and indirectly in the processes of mixed infection and intoxication are no less elusive in their mode of action Even where substantial grounds exist for the tentative explanations of such toxic phenomena there remain the reflex and mutual play of reactions between the various systems of the organism integrated by a nervous mechanism varying in its sensitiveness under both normal and abnormal conditions and activated in its functions by internal secretions whose properties and conditions of production are obscure even in normal states and whose behavior under abnormal conditions is even more obscure

The Myocardium —A clear conception of the structure of the cardiac musculature is essential to an understanding of its diseased states and their

significance. Although it originates as a thickly meshed reticulum of mesenchymal cells with their bodies in regular contact with each other, the heart muscle is a syncytium whose striated fibrils run through the reticulum regardless of the so-called cell boundaries. These boundaries or intercalary discs are interposed in the course of the continuous fibrils which unite the cells into fibers; the fibers branch and their branches unite neighboring fibers into the syncytial structure of the finely transversely striated cardiac musculature. A very fine connective tissue surrounds the reticulum. The amount of the connective tissue increases normally with advancing years and is always more prolific in the auricles than in the ventricles. The fibers of the ventricles possess a constancy in size and structure compared with those of the auricles, in which the fibers are usually thicker and more varied in appearance. Distinct in appearance, site and function is the specialized musculature of the heart, the sino-auricular and auriculo-ventricular systems, which are concerned with the initiation and regulation of its coordinated contraction; this special muscle is poor in the development of its striation and is rich in glycogen. When stained with the Van Gieson stain it is paler than the contractile muscle and its fibers are surrounded by a relatively large amount of connective tissue. The fibers show an intimate connection with nerve structures, and in the main course of the two systems before they enter into intimate association with the ordinary musculature they are separated from that musculature by layers of connective tissue. One system, the sino-auricular special muscle or node of Keith and Flack, is situated in the sino-auricular groove, and in the region of this node the first demonstrable signs of cardiac contraction take place. The other system of special muscle, the auriculo-ventricular node and bundle, is situated in the inter-auricular septum on the roof of the inter-ventricular septum just in front of the coronary sinus. This node is continued into the main auriculo-ventricular bundle which runs along the roof of the inter-ventricular septum till it reaches the septum fibrosum, where it divides into the right and left main branches, and these branches run down on either side of the inter-ventricular septum beneath the endocardium and separated from the ordinary musculature by fibrous tissue; their arborizations come into association with the contractile muscle as they approach the trabecular and papillary muscles of the ventricles. It is important to recognize the special site and function of these systems of coordinating musculature, inasmuch as certain degenerative processes in the heart depend not so much on the extent as on the location of the disease.

After the first year of life small masses of pigment appear at the poles of the muscle nuclei. These pigment granules stain with osmic acid and with Sudan III and may be mistaken for fat. They possess no pathological significance.

There are two subjects of controversy which may be disposed of here. Much has been written about segmentation and fragmentation of the cardiac muscle fibers, by segmentation being understood an interruption of the continuity of the fibers at the intercalary discs and by fragmentation a discontinuity between the discs. The former is exceedingly rare and the latter is very frequent in advanced years and does not occur in infants; the latter possesses no pathological significance; it is an agonal incident whose condition is probably related to the occurrence of the extreme contraction or distension of the organ at the time of death. The second subject of controversy has arisen from the conception of the heart as a parenchymatous organ like the kidneys or liver. Basing his observations on this conception Albrecht and his followers have attempted to explain enlargements and weakness of the heart as being due to a compensatory effort to make good the defect due to chronic inflammation of the organ. But the heart is not a cellular organ in the same sense as the kidney or the liver. It is composed of muscle fibers united to each other by branching and only such observations as are based on a recognition of this elementary fact require attention.

1 *Albuminous Degeneration* —In all infectious and toxic states there is likely to occur albuminous degeneration or cloudy swelling of the muscle fibers which is difficult to distinguish from post mortem degeneration. This consists in the deposit of albuminous granules between the fibrils which disappear on the addition of dilute acetic acid. The muscle substance appears to the naked eye cloudy and less transparent than in the normal state. It has a somewhat dirty appearance and is flabby and easily torn. The kidneys and liver exhibit corresponding changes. Nothing is known of the clinical significance of these regressive metabolic processes except that they occur in febrile and toxic conditions.

2 *Fatty Degeneration* —Fatty degeneration of the cardiac muscle shows itself microscopically either in the diffuse form of a yellowish muddy discoloration of the musculature or in a patchy form best seen on the endocardial surface, where it presents the characteristic thrush breast appearance. Microscopically the fat droplets are arranged in rows between the muscle fibrils with larger droplets in the perinuclear sarcoplasm. It is not associated with gross destruction or disturbance of the muscle structure and is most marked in anemias, phosphorus poisoning, acute yellow atrophy of the liver, and in some conditions of chronic heart failure. Its clinical importance has been much overestimated in infectious and toxic states. It does not at any rate appear in a degree sufficient to exercise a determining influence on the course of events.

Fatty infiltration is quite distinct from fatty degeneration and consists in a proliferation of epicardial fat which, when excessive, infiltrates the

spaces between the muscle bundles of the heart especially in the region of the conus of the right ventricle It occurs in persons showing other evidences of adiposity It has no association with infectious or toxic processes although it may exercise a baneful influence on the cardiac strength and render the heart more liable to premature exhaustion in toxic states At any rate it has been held responsible for cardiac failure in chloroform narcosis

3 *Vacuolar Degeneration*—This form of degeneration occurs for the most part in cases of chronic valvular heart disease It is more pronounced in the auricular than in the ventricular fibers Both fatty and vacuolar degenerations are associated with edema and with defective circulation and oxygenation and are seen in the secretory cells of the kidney It is of no importance in the present study

4 *Waxy and Hyaline Degeneration* This consists in homogeneous clumping of the content of the muscle fiber complete destruction of its structure and the abolition of its function and is the most important form of metabolic degeneration found in acute infectious and toxic processes it occurs in diphtheria and typhoid fever and occasionally in pyemic infection in which condition it is occasionally seen also in the somatic musculature

5 *Necrosis*—Necrosis occurs in the neighborhood of septic infections due to emboli in pyemic states Its clinical significance for the heart depends upon its site and extent but in the long run it is of course only one evidence of what is usually a fatal infection Necrosis may occur also in infarction due to emboli from non pyogenic valvular vegetations or it may be due to a defective blood supply from narrowing of the coronary arteries a condition for which syphilis is for the most part responsible

It has been deemed necessary to make the foregoing reservations and explanations in order to be able to define precisely the contribution which pathological anatomy can make to the solution of our problem However important it may be to find in altered structure an explanation for a disordered function that explanation loses its validity unless the limits within which it is applicable be accurately defined It should be clearly understood that while some circulatory disabilities in infectious and toxic processes can be correlated with structural alterations and disintegrations there are others which cannot and it is the business of the observer to discriminate in the first place which are and which are not and in the second place to extend as far as it is possible the field of the known into that of the unknown It remains now to consider separately the phenomena included under myocarditis endocarditis peripheral degenerations in the circulatory system in infectious and toxic processes peripheral disturbances in the circulation in infectious and toxic processes the effect on the circulation of extra circulatory conditions incident to infectious and toxic processes and finally the

circulatory relations of certain infectious processes of particular importance in relation to the circulation: rheumatism, diphtheria, syphilis, and acute infectious endocarditis.

Myocarditis

1. *Simple Acute Myocarditis*

The term "myocarditis" applies here exclusively to conditions in which the myocardium is the seat of inflammatory reaction. It is characterized by cellular infiltration and proliferation of the interstitial tissue accompanied, not infrequently, by degenerative processes of the substance of the muscle fibers, and in many cases, by the disappearance of the contractile elements (waxy degeneration). In some cases the reaction occurs in isolated masses and in others it is diffuse. In most cases, it is most marked in the neighborhood of small vessels, and in others, it predominates in the interstitial tissue between the muscle bundles.

Mononuclear and polymorphonuclear leucocytes, and plasma cells appear in varying proportions in different cases. Variations in the size, shape and affinity of the muscle nuclei for alkaline dyes constitute a prominent feature, although such variations are seen also in hearts which exhibit patchy fibrosis due to defective coronary circulation. Enlargement of the nuclei is an evidence of retrograde change due to defective nutrition, and not, as has been suggested, the sign of compensatory hypertrophy. Interstitial infiltration may be quite independent of parenchymatous degeneration; perivascular, intramuscular and sub-endocardial inflammation may occur without any evidence of the retrograde metabolic changes which indicate destruction of muscle fibers. In diphtheria, for example, one may find extensive inflammatory reaction without serious involvement of the contractile tissue, while diffuse waxy change may occur without interstitial reaction, to begin with at least. On the other hand, cases are seen in which the parenchymatous and connective tissue changes are both present in varying degree. Occasionally the perivascular and perineuritic infiltration constitutes a special feature of the anatomical picture.

The foregoing description applies more particularly to the forms of myocarditis seen in diphtheria and very occasionally in typhoid infection. In marked contrast with this, and easily distinguished from it, is the lesion which is characteristic of the carditis of rheumatism and chorea. This latter consists in an interstitial and sub-endocardial distribution of submiliary nodules, whose outstanding feature is the radial or fan-shaped arrangement of connective tissue cells with large clear nuclei. The nodule are oval in shape, often surrounded by fibrin and in close association with perivascular tissue. Small areas of necrosis and giant cells may be found in

the center of the nodule which may be surrounded and infiltrated by other cellular elements of the nature of lymphocytes granular leucocytes and plasma cells The lesion of recent rheumatism of the heart cannot be distinguished from that of recent rheumatic fibrositis or myocarditis in the skeletal structures It is in each case essentially an involvement of the connective tissue although in many instances the adjacent muscle fibers may be affected While the myocarditis of diphtheria and typhoid shows itself for the most part in the degeneration and destruction of contractile elements the myocarditis of rheumatism is for the most part a fibrositis and shows itself in a typical infiltration of the tissue outside of the muscle bundles

These two types of inflammatory reaction as exemplified in diphtheria and typhoid on the one hand and in rheumatism on the other may be observed also in skeletal muscle the former being seen most frequently in the abdominal muscles in typhoid fever as waxy degeneration and the latter in the acute fibrositis or fibromyositis of rheumatism in the somatic musculature especially in the trapezius lumbar gluteal and pectoral muscles It should be pointed out however that while the waxy degeneration of the abdominal muscles in typhoid is accompanied by interstitial reaction there has not yet been described in these muscles a form of degeneration corresponding to the acute interstitial and intramuscular myocarditis of diphtheria with its diffuse destruction of contractile substance

Arising from specific and contributory causes and exhibiting each a distinct structural reaction these forms of myocarditis may be compared in the course which they run and in the effects which they ultimately exercise on the heart The diphtheritic type if it does not lead to death progresses within a few weeks to a final fibrosis of the affected areas The waxy fibers become absorbed and are replaced by cicatrices Other fibers which have been partially digested in the inflammatory reaction are absorbed in the process of healing and the interstitial granulations contract and harden into fine connective tissue bands Once cicatrization has been completed a final stage in the process of healing has been reached unless of course in the unlikely event of reinfection The liability to subsequent cardiac failure depends exclusively on the initial damage to the heart and on the advent of new features outside of the range of the diphtheritic infection The original damage however may have been so great as to lead to permanent disability which may show itself in the ready exhaustion of the patient slight dilatation of the heart with mitral incompetence and occasional irregularity of its action The reserve force of the organ may be so diminished as to render impossible the exertion and activity of a normal physiological life and although the disease is not progressive in a histological sense the original damage may be a determining factor in the production of cardiac failure in the course of a subsequent infection of another kind

In the case of rheumatic myocarditis the muscle fiber is not so seriously affected and the immediate danger is not so great but the period of recovery is more uncertain With the passing of the acute phase the nodules and interstitial granules become fibrosed In the case of diphtheria one may be fairly certain that in three or four months from the onset of infection the progress of the disease has been arrested while in the case of rheumatism there is constant liability to recurrence Endocardial rheumatism may have occurred although in recent cases the signs of the are equivocal A mitral systolic murmur may be the evidence of dilatation only but it may also be the indication of an organic lesion constituting the original focus of later developments So tenacious is the poison of rheumatism that once having found a seat in the heart the probability is that it will recur if not in one form at least in another

2 *Acute Septic Myocarditis*

This condition arises as a complication of septicemia or pyemia and may or may not be associated with ulcerative endocarditis When it is due to showers of minute emboli there are multiple abscesses of microscopic dimension when it is associated with ulcerative endocarditis there may be larger and isolated emboli in the coronary arteries producing abscesses of considerable size which may break into the cardiac chambers or even produce rupture of the heart wall The cardiac signs are of course overshadowed by the other evidences of pyemia and the prognosis is always grave

3 *Acute Idiopathic Myocarditis*

This is a form of acute interstitial myocarditis of unknown origin It runs a rapid and usually a fatal course It presents the signs and symptoms of a general infection and on post mortem examination the only gross evidence of disease is in the myocardium There is a patchy necrosis of muscle with diffuse interstitial infiltration The histological picture resembles in many states that of an acute rheumatic myocarditis although in a more extensive and intensive form than that observed in acute rheumatism The cases are usually fatal

4 *Syphilitic Myocarditis*

Diffuse interstitial fibrosis of the myocardium is not uncommon in congenital syphilis It is comparable with the fibrosis which is seen in other highly developed organs in that condition

In acquired syphilis lesions of the myocardium are rare in comparison with the frequency of infection Such lesions may take the form of isolated gummata or of interstitial fibrosis chiefly in the perivascular area Occasionally the specialized conducting system of muscle auriculo ventricular

node and bundle may be involved in a lesion spreading from a syphilitic aortitis and giving rise to the well known clinical phenomena of heart block. The most serious disability to which the myocardium is exposed in syphilis is that due to lack of nutrition from the narrowing of the coronary arteries in the proliferative reaction of aortitis. The gross evidence of this may be seen in the patchy fibrosis which represents areas of anemic infarction. Such areas are not in themselves so much a source of myocardial weakness as an evidence of the impoverished state of the organ as a whole.

5. *The Myocardium in Tuberculosis*

Apart from the miliary nodules which occur in acute miliary tuberculosis, tuberculosis of the myocardium is exceedingly rare. Very occasionally caseous nodules have been observed, and a tuberculous process may spread from the pericardium to the outer surfaces of the cardiac muscle. Tuberculosis of the myocardium has no clinical importance.

6. *Chronic Myocarditis*

This term is frequently employed without any underlying conception as to its precise meaning. There is no such disease as chronic myocarditis comparable with chronic nephritis or with cirrhosis of the liver or with the chronic syphilitic cerebritis of general paralysis of the insane. If the designation be applied to rheumatism or syphilis of the heart, then that should be done on the clear understanding that one or other of these diseases is present. Fibrosis of the cardiac muscle may, as has been pointed out, result from the poverty of the coronary circulation, or it may be the result of a diphtheritic, typhoid, rheumatic or syphilitic lesion which has spent itself; but, in any case, the term is a general one and has no relation to any specific process outside of the various inflammations which have already been discussed.

7. *The Myocardium in Acute Infection*

The myocardium in pneumonia, scarlet fever, measles, smallpox, typhus and gonorrhea may possibly be affected by toxic agencies, but there is no anatomical evidence to show that myocarditis in the sense in which the term should be implied occurs in these diseases. In the febrile period the circulation is disturbed. The heart's action may be rapid or abnormally slow or even irregular; the cardiac chambers may be dilated and there may be mitral incompetence. The sounds may be impure and soft, but the probability is that these abnormalities are the transient effects of the toxins of the infection, not only on the heart itself but on the regulatory system of the circulation as a whole, and not due to any structural alteration of the myocardium comparable with the lesions which are characteristic of myocarditis as described above.

ENDOCARDITIS

For practical purposes the term endocarditis is applied to inflammatory states of the valvular endocardium although the process may occasionally spread to the mural endocardium and to the chordae tendineae For descriptive purposes it is convenient to consider the subject under the arbitrary divisions

1 Simple verrucose endocarditis
2 Acute ulcerative endocarditis
3 Subacute ulcerative endocarditis and
4 Chronic endocarditis

1 *Simple Verrucose Endocarditis*

This consists primarily in necrosis of the endothelium of the valves confined to those areas or parts of the areas of the valves which come into contact on closure On the basis of this limited necrotic softening small excresences of fibrin are deposited from the blood Blood platelets white and red corpuscles and fibrin constitute the composition of the row of minute transparent grayish white granules which form a narrow ring around the surfaces of contact of opposing valves Microbes circulating in the blood are not infrequently deposited on the surface of these thrombotic masses but these organisms judging from their superficial position have no causal relationship to the condition This simple form of endocarditis is found in the last stages of the cachexia of ulcerating tumors chronic nephritis general tuberculosis and other wasting diseases in which the metabolism of the organism is perverted and its resistance low It is an occasional post mortem feature in pneumonia and enteric fever where it probably originates in the moribund state

Indistinguishable from this in its original appearance but totally different in its significance in regard to possible developments is the initial stage of rheumatic endocarditis This condition begins as described above in the form of grayish white granules on the surfaces of contact of the closed valves most frequently on the mitral sometimes on the aortic seldom on the tricuspid and practically never on the pulmonary valves In some cases there may be a sand like dispersal of the granules on the chordae tendineae or on the pars membranacea In the early stages they are easily rubbed off Gradually the valve structures in the neighborhood of the deposit show a reaction in the form of increase and enlargement of the connective tissue cells The granules become firmer and less easily dislodged Continuation of the process may lead to a confluent attachment of the adjacent corners of the valves to each other and to adhesions between adjacent chordae tendineae the valvular tissue is not vascularized and in the early stage

there is no true inflammatory reaction If at this stage the process becomes spent the granules may become hyaline or calcified and the disease may pass off leaving the valves damaged but slightly in the anatomical sense and functionally unimpaired But the virus of rheumatism is pertinacious in its attachment to the tissue in which it has once gained a seat There may be a remission in its activity but it is apt to reassert itself A recurrence is accompanied by a renewal of valvular deposit more extensive disintegration of the valvular structure and perhaps by a true inflammatory reaction on the part of the blood vessels at the base of the valves Should this latter contingency arise a process of vascularization of the valves produces an ultimate organization of the thrombi Once this stage has been reached the fate and ultimate efficiency of the valvular apparatus is compromised Granulation is followed by cicatrization and its attendant consequences In the case of the mitral valve the cusps become hard and thickened the chordae tendineae become shortened and the adjacent cords may granulate into a coherent mass Progressive cicatrization is attended by increasing deformity of the valvular mechanism the orifice becomes narrowed auriculo ventricular flow is impeded and the shortened chordae tendineae and thickening of the cusps render effective closure impossible during ventricular systole In the case of the aorta the free edges of the cusps become thickened rolled in and retracted and valvular competence during ventricular diastole is rendered defective Such mechanical defects are however made good to a large extent by compensatory hypertrophy of the cardiac musculature The extent to which this is possible depends upon the degree of valvular defect and upon the condition of the muscle itself Even a normal cardiac muscle like other muscles of the body has only a limited capacity to meet abnormal demands and in the case of rheumatism as has been noted above the musculature is not infrequently itself the seat of pathological reaction This holds good in spite of the fact that the main evidence of the activity of the rheumatic poisoning is found not in the protoplasm of the muscle fiber but in the interstitial and sub endocardial layers which though not contractile contain elements which are no less important to the normal activity of the cardiac action Prejudiced by valvular incompetence drawing disproportionately on the reserve strength of a diseased or even healthy contractile mechanism and constantly exposed to the possibility of a recurrent poisoning it is not difficult to imagine the precarious state and limited possibilities of the subject of rheumatic endocarditis If on the easy routine of life there be imposed undue physical or mental exertion or the burden of pregnancy it is easy to imagine the premature exhaustion of the limited amount of reserve On the other hand the course of the disease may be interrupted and the disability aggravated by incidental pericarditis pleurisy with effusion nephritis or pulmonary or brain embolism

Progressive constriction of the mitral orifice may lead to hypertrophy of the auricular muscle with subsequent muscular degeneration and such degeneration may be accompanied by paralysis of the auricular function with its well known clinical signs Further discussion of this aspect of the question does not belong to our subject

2 *Acute Ulcerative Endocarditis*

This form of endocarditis is due to pyogenic infection of the valve In its early stages and especially in acute and fatal septicemias it presents appearances which are not readily distinguished from those of simple verrucose endocarditis described above Depending upon the virulence of the infection and upon the length of time in which it is in process the changes in the valves may vary from a condition in which there is merely a narrow row of granular deposits on the edges of contact during closure to a condition in which the apertures are partially closed by the growth of large fungoid or polypoid thrombi In rapidly progressing septicemias small opaque granules of a dirty yellow color are deposited on the auricular surfaces of the mitral or on the ventricular surfaces of the aortic valves As a rule they are more irregular than the corresponding excrescences seen in the simple verrucose type and in the region of the lesion the valve presents a dry and raw looking appearance A smear preparation from the lesion shows large numbers of micro organisms Should the process be prolonged large thrombi develop on the bases of these initial lesions The ulcerative process may extend onto the cardiac walls The valves may be perforated the aorta may be invaded with destruction of its wall causing the formation of aneurysm or rupture The thrombi on the aortic valves may be so large as to produce a partial or complete occlusion of a coronary artery The chordae tendineae may be severed and float freely in the ventricular cavity and even portions of the mitral valve may be separated from the main structure The main stem of the auriculo ventricular bundle may be invaded by an extension of the process either from the aortic or from the mitral valve thus giving rise to an interruption of the auriculo ventricular rhythm Interference with the valvular competence by the extension of the ulcerative processes may lead to rapid failure of the heart from mechanical causes

The more remote effects of the condition depend upon the character of the local reaction and especially upon the consistence of the thrombotic masses If the masses are soft necrotic and fragile then a dispersal of emboli laden with pyogenic microbes gives rise to miliary abscesses all over the body The symptoms of the spread will depend upon the location of the secondary infections In the unlikely event of a subsidence of the acute valvular infection the resulting process of healing and cicatrization will

leave a deformity and deficiency of the valvular apparatus more severe than that seen in the usual forms of chronic endocarditis

3 *Subacute Ulcerative Endocarditis*

Infective endocarditis may run a chronic course In that event it is *usually due to a pyogenic infection imposed upon an old valvular defect* The anatomical changes consist in indolent ulceration of the affected valve and spread of the process into the adjacent structures The micro-organisms are situated deep in the base of the ulceration and there is practically no tendency to the production of thrombotic masses which are characteristic of the more acute kind These cases may go on for months with anemia weakness and obscure fever giving rise to an extremely puzzling clinical problem This aspect of the question is dealt with later on

4 *Chronic Endocarditis*

The chronic endocarditis of rheumatism and the subacute or chronic form of infective endocarditis have been discussed elsewhere The only other form of chronic endocarditis of infective or toxic origin remaining for discussion is that due to syphilis Syphilitic endocarditis arises in association with syphilitic aortitis and this is fully discussed later on

Peripheral Degenerations in the Circulatory System in Infectious and Toxic Processes

While the arborizations of the cardiovascular system participate in the functional disorders which constitute the circulatory reactions to infectious and toxic processes there is no evidence to show except in the case of syphilis that the vessels themselves are the seat of organic changes In most febrile states the vasomotor tonus is relaxed and the character of the pulse wave assumes the well known dicrotic quality Attempts have been made to correlate the incidence of acute infections with the later development of arteriosclerosis Fatty changes in the intimal endothelium have been regarded as a prelude to later sclerosis It may be said with confidence however that much evidence is still required to establish the validity of this thesis In the case of diphtheria and of rheumatism attention has been called to the fact that the inflammatory reaction in the myocarditis of these diseases finds its seat of preference not infrequently in perivascular areas It can scarcely however be maintained that adventitial changes such as do occur in these conditions are the source of disturbances which are prejudicial to the course of the disease

It sometimes happens however, that involvement of vessels does occur as an incident in the infectious process In ulcerative endocarditis for example the media of the aorta may become the seat of purulent infiltration giving rise to aneurysm and even to rupture Septic emboli from an ulcerative endocarditis may find their way into cerebral arteries and there give rise to aneurysm and hemorrhage Local pyogenic infections may lead to septic thrombosis of neighboring veins and the dislodgement of septic thrombi may be the determining incident in the development of pyemia Complications of this character are not infrequently met with in mastoid disease and in puerperal sepsis Very occasionally the ulcerative angina of scarlet fever may eat its way into the large vessels of the neck and give rise to fatal hemorrhage But when these accidental complications are excluded it may be said that the ordinary acute infections run their course fatally or otherwise without involvement of the extra cardiac part of the circulatory system

Tuberculous disease to which no tissue of the body is immune occasionally finds the seat of reaction in blood vessels This does not occur however in the same way or to the same extent as in syphilis It may be said that in tuberculosis the vascular lesion is accidental and its more serious complications extremely rare In tuberculous meningitis there are infiltrations of the adventitia and media and frequently also endarteritis In this respect tuberculous meningitis bears some resemblance to syphilitic meningitis The most serious tuberculous complications in the vascular system are however those in which the veins are invaded by a spread from disease in neighboring lymphatics In a considerable proportion of cases acute miliary tuberculosis is due to the formation of tuberculous thrombi on the intima of veins which are invaded from neighboring tuberculous bronchial gland and occasionally the miliary spread may be found to originate in a similar invasion of the thoracic duct A vascular incident which sometimes occurs in tuberculosis is the rupture of an aneurysm in a tuberculous cavity the aneurysm originating from the erosion of the vessel wall by the ulcerative process

The importance of syphilis in lesions of blood vessels is considered fully at a later stage (p 326)

PERIPHERAL DISTURBANCES IN THE CIRCULATION IN INFECTIOUS AND TOXIC PROCESSES

Reference has already been made to the misleading tendency to look upon the heart as the sole organ of circulation and to forget altogether, or to regard as negligible the part played by its arborizations in the maintenance of nutrition In the evolutionary process the heart has undergone mor

phological and histological differentiation which enables it to propel the proportionately larger quantities of blood which are demanded by the tissues of animals whose life and metabolism have become more active. But such developmental adaptation is not confined to the heart: the blood vessels, arteries and veins exhibit a progressive differentiation in structure which may be taken to imply an increased capacity to meet the needs of a more varied and more strenuous existence. Even in the development from the horizontal to the upright posture some regulatory adaption of the peripheral circulation must have occurred to avoid a disproportionate distribution of blood. To what extent the peripheral circulation is propulsive and to what extent it is merely regulatory in its distributive function can only be surmised. In health the whole system works so smoothly, its organic elasticity is so accommodating that the intricacy of the nervous and chemical factors by which it is integrated cannot be comprehended. There are incidents in infectious and toxic processes, however, which are not explained by degeneration or exhaustion of the cardiac muscle or by interference with the intracardiac regulatory mechanism.

A girl of ten years convalescing from diphtheria a month from the onset of signs of infection suddenly becomes extremely pallid and restless. Apart from occasional irregularity of the pulse which has been noticed for two days no premonitory signs are observed. The pallor and restlessness remain, the pulse becomes rapid and there is occasional vomiting. There is tenderness over the liver and albuminuria appears. Without dyspnea or cyanosis or edema death occurs a week after the onset of the complication. On post mortem examination an interstitial myocarditis is found: the inflammatory reaction predominates in the spaces between muscle bundles and around the muscles; there is only slight degeneration and destruction of muscle fiber. There is great congestion of abdominal viscera, especially of the liver. This must be a common experience to those who have had fever hospital experience. The clinical type may of course vary greatly: the patient may die suddenly without having previously shown evidence suggestive of cardiac weakness; on the other hand the illness may be prolonged over several weeks, with periods of pallor, restlessness, in some cases apathy and sickness alternating with periods of comparative well being, and in the end the patient dies or very occasionally recovers.

This condition is not confined to diphtheria. We have seen it on three occasions in rheumatism. A girl twelve years of age, in the fifth week of convalescence from rheumatic fever, exhibited a sudden change in the course of recovery. The high temperature of the initial fever had subsided in three days, but there was an occasional rise from time to time up till the onset of the complication referred to. The heart was slightly dilated to the left, a mitral systolic murmur was present and

myocarditis was suspected The main features of the new development were extreme pallor sudden rise in rate of pulse from 90 to 120 per minute with fall in the pulse tension and extreme restlessness she complained of pain over the heart there was no dyspnea, no cyanosis and no sign of pulmonary congestion the pallor and restlessness continued albumin appeared in the urine and there was tenderness on pressure over the liver There was occasional sickness The picture was typical of that seen in diphtheria so much so that in spite of the rheumatic fever diphtheria was suspected She died on the fifth day of the complication and post mortem examination revealed the characteristic lesion of rheumatic myocarditis The nodular infiltration was most extensive around the vessels in the fibrous septa between the muscles and in the sub endothelial tissue of the left ventricle There was a recent endocarditis of the mitral cusps But this had no importance from the point of view of mechanical efficiency The heart was flaccid and dilated and there was intense vascular enlargement of the abdominal viscera

There occurred in each of these cases a well defined series of clinical phenomena which commenced unexpectedly in the course of the disease sudden pallor restlessness and sickness rise of pulse rate with albuminuria and enlargement of the liver but without dyspnea cyanosis or edema These are not the signs of cardiac failure in the strict sense in which the term is employed clinically They are the signs of shock and the post mortem evidence pointed conclusively to the draining of the blood into the splanchnic circulation with the consequent superficial pallor anemia of the brain and insufficient supply of blood to the heart to stimulate the normal rate of contraction Call it shock call it what one may the condition is essentially the same as that which sometimes follows a severe wound, or that which follows dilatation of the sphincter in the operation for hemorrhoids or that which occurs occasionally during the excision of a tuberculous knee joint or during operation for circumcision It is suggested that stimuli passing from the diseased heart so influence the vasomotor control as to produce the determination of an unduly large proportion of the blood to the abdominal vessels and viscera It may be objected that this is an extremely rare occurrence but so is acute myocarditis apart from diphtheria and rheumatism and the peripheral disturbances described are by no means an infrequent complication of diphtheria It is probably also the most frequent complication in those cases of acute rheumatism where the patients die early and unexpectedly in the course of the disease Whether and to what extent and in what manner the peripheral circulation is disturbed by or adapted to or compensated for in chronic disorders of the heart are not problems which concern us here that they are problems of first rate importance cannot be denied

The Effect on the Circulation of Extra Circulatory Conditions Incident to Infectious and Toxic Processes

The maintenance of an effective circulation depends not only on the normal structure and activity of the circulatory apparatus itself but also *on the effective cooperation of accessory forces which assist in the propulsion of blood* Chief among these is the mechanism of the respiratory movements and any infection or disease which compromises the freedom of respiratory movements throws an embarrassment on the circulation In acute lobar pneumonia for example it is extremely difficult to estimate the importance of the various factors which contribute to a fatal issue

The infected patient is subjected to the adverse influences of a complicated series of abnormal processes which for the sake of convenience may be termed chemical and mechanical The chemical agencies in addition to oxaemia include the disintegrating bacteria the local products of the reaction between the micro organisms and the host and various other substances of abnormal quantity or quality which originate as a result of the interference of toxins with the normal metabolism in parenchymatous organs These processes *manifest themselves in well recognized anatomical* changes in the liver the kidneys and the cardiac muscle and the clinical manifestations of the disease indicate a reaction on the part of the nervous system also The degree to which the parenchymatous organs are affected depend on the amount of abnormal chemical substances present and the affinity of these for the affected organs The progress of the disease will be determined largely by the reaction of the bone marrow and other tissues which supply the anti substances necessary to hold the noxious chemical processes in check The issue of pneumonia however may be influenced by the mechanical conditions incident to the disease The pain of the pleurisy interferes with free movement of the chest wall and an extensive consolidation too limits the expansion of the thoracic cavity and creates an obstruction to the pulmonary circulation the work of the right ventricle is thus increased and the efficiency of the organ may be seriously prejudiced

However it is in the case of those conditions which are classed collectively as bronchopneumonia in children that mechanical difficulties are most pronounced Rapid respiration and cyanosis are common features of bronchitic affections more especially when accompanied by rickets and atelectasis In many of the cases the toxic effects of the pneumonia are much less serious than the physical disability under which the heart suffers in maintaining the circulation An extensive clinical and correlated post mortem experience has established this fact beyond all doubt

Within very narrow limits the healthy heart preserves a definite shape and size varying only with the weight and age of the individual There

occur however in certain pathological conditions well recognized modifications of shape and size In chronic Bright s disease the left ventricle becomes greatly enlarged The nature of this enlargement and change of shape is fairly constant and gives an abnormal shape to the pathological heart Aortic and mitral disease are also responsible for enlargement and change of shape more or less characteristic of the disease the heart of aortic regurgitation for instance is known as the 'cor bovis Where there is tuberculous adhesive pleurisy or chronic fibrotic phthisis the right side of the heart is often enlarged and a similar variation is not infrequent with chronic bronchitis and emphysema Now with the exception of the latter cases the cardiac change is associated with an interference with the normal dynamic conditions inside the vascular system itself On the one hand the peripheral blood pressure is increased by the vaso constriction of chronic Bright s disease or by changes in structure of the smaller vessels in arterio sclerosis or on the other hand the mechanical efficiency of the pumping apparatus is compromised by the valvular defects in the cardiac apparatus itself and the enlargement is the result of an attempt to compensate for this defect When however a change in the size and shape of the heart is observed in an otherwise normal vascular system associated with advanced disease of the lung or chest wall one has then to deal with the result of extraneous influences with the effect on the vascular apparatus of forces from without and the extent to which an interference with normal pulmonary expansion can be correlated with increase in the size of the heart may be taken as indirect evidence of the part played by the normal respiratory movements as factors which make for an efficient circulation

The circulatory burden of respiratory difficulty is most frequently observed in (1) extensive collapse of the pulmonary tissue (atelectasis) and (2) in rachitic or tuberculous deformity of the thoracic cavity

(1) Cases Illustrative of Atelectasis and Cardiac Failure

Case 1 —A girl of seven and a half years fairly well developed had a severe diphtheria followed by paralysis of the muscles of deglutition An aspiration pneumonia was supposed to have followed and after eight weeks illness she died For a fortnight previous to her death she was very pale and suffered from breathlessness and for some days before death there was edema of the lower limbs Post mortem examination showed very extensive atelectasis in both lungs the right upper lobe and the left lower lobe being completely collapsed while the remaining lobes were greatly distended The child weighed 3 stone (42 lb or 19 kilos) and the heart weighed 7½ oz (212 6 gm) The form of the heart was abnormal It was broad proportionately at the base of the ventricles and rounded or almost flattened at the apex and both ventricular walls were hypertrophied The venous

system was engorged and the parenchymatous organs showed signs of passive venous congestion The cardiac muscle showed no signs of fatty or fibrotic degeneration

Case 2 —A boy of two years was admitted to the hospital suffering from bronchopneumonia He died after an illness prolonged over ten weeks He was fairly well developed and the chest was of normal shape During the last two months of illness he was pale and his respirations were rarely under 50 per minute and sometimes were 80 per minute The pulse ranged between 140 and 160 per minute While at the beginning of his disease the temperature varied between 101 and 103 6 F for a period of a fortnight during the last six weeks there was no febrile disturbance beyond an occasional rise of temperature to 101° and 102 F For a few days before death there was oedema of the lower limbs Post mortem examination in this case showed the heart to be enlarged and relatively broad over the whole extent of the ventricles The interventricular septum as demarcated by the descending coronary artery occupied a relatively normal position The heart weighed 4 oz (113 4 gm) and the body weighed 22 lb (9 9 kilos) On opening the heart both the ventricles were found to be hypertrophied The shape of the heart was abnormal with great hypertrophy of the walls more especially of the right ventricles and the septum On microscopic examination the cardiac muscle showed no signs of fatty or fibrotic degeneration The lungs were collapsed along their posterior portions and at places along the anterior margins Microscopical examination showed that the pathological lesion was one of collapse While the evidence of old bronchopneumonia was still present the process was no longer an acute one and there was no sign of recent inflammation There was great engorgement of the whole venous system and passive congestion of the parenchymatous organs

(2) *Cases Illustrative of Chest Deformity and Cardiac Failure*

Case 1 —A girl eight years of age with very extensive rickety deformity of the chest and lower limbs was admitted to the hospital on account of breathlessness While under observation extending over five weeks she had no abnormal rise of temperature The chest movements were described as being restricted in the upper part of the thorax The respirations numbered 30 to 50 per minute and the pulse from 130 to 150 per minute Post mortem examination showed that the heart weighed 7½ oz (212 6 grams) while the body weighed 30 lb (13 6 kilos) The heart was of firm consistence relatively broad and with a somewhat rounded broad apex and short in length from the apex to the base of the ventricles On opening it was seen that both ventricles had participated in the hypertrophy although the most marked hypertrophy was that of the interventricular septum The

right auricle was dilated. The cardiac muscle showed no signs of fibrotic or fatty degeneration. The lungs were greatly distorted in shape. The anterior margins were collapsed and a line of depression was present on the anterior surfaces corresponding to the site of junction of the ribs with the costal cartilages. The distortion of the lungs at this line of depression was so great as to give the anterior borders the appearance of being tilted forward about 45 degrees from their normal position. The anterior borders were airless and there was considerable collapse on the posterior aspects of the upper lobes of both lungs. There was no evidence of acute inflammation in the lungs. Examination of the thoracic cavity showed a striking deviation from the normal. It was greatly contracted in its upper half, and this contraction was due to an in sinking of the ribs along the line of their junction with the costal cartilages. It was as if pressure had been exercised along this line on either side in a direction downwards and inwards so as to produce an approximation towards the middle line and an obliteration of the upper and anterior part of the thoracic cavity. Towards the diaphragm the cavity widened and the line of depression gradually disappeared. The ribs were firm and well ossified. There was general venous engorgement and passive congestion of the parenchymatous organs.

Case 2.—A boy of one and one half years had an extreme rickety deformity of the chest. The chest was of the fiddle shaped type, very much contracted at the level of the axilla and expanded at the insertion of the diaphragm. Respirations were rapid and shallow, varying from 50 to 80 per minute, and the pulse rate was from 150 to 180 per minute. The respiratory movements were confined almost entirely to the abdomen and lower part of the thorax. For a week before death there was edema of the lower limbs. Post mortem examination of this case showed an abnormal size and shape of the heart. The organ was of firm consistence. It was broad at the base and relatively short from the apex to the base of the ventricles. The apex was rounded off in the arc of a very large circle. The anterior interventricular groove was not displaced relatively. The right auricle was greatly distended. A transverse section through the ventricles showed marked hypertrophy of the walls of both chambers, more especially perhaps of the right ventricular wall and the interventricular septum. The shape and degree of the hypertrophy of the heart resembled almost exactly the condition seen in Case 2 under atelectasis, where there was extreme collapse following a bronchopneumonia but no deformity of the chest wall. In this case the heart weighed 3½ oz (99.2 grams) and the body weight of the child was 21 lb (9.5 kilos). There was no fatty degeneration or fibrosis of the cardiac musculature. The lungs were distorted, the anterior portion being marked off by a deep furrow which corresponded in site with the line of junction of ribs with costal cartilages. There was a considerable degree of collapse along the anterior margins in

front of the furrows and there was also extensive atelectasis in the posterior portions of both lungs more especially in the upper lobes There was no evidence of recent inflammation The thoracic cavity was very much diminished in extent The only portions which retained their normal contour were the recesses on each side of the vertebral column posteriorly The anterior mediastinum was almost obliterated by the in sinking of the ribs along the line of the rosary The thoracic cavity was enlarged on the plane of the diaphragmatic attachment The ribs were soft and pliable and could be bent like green wands They contained practically no true bone substance It was possible to cut microscopical sections of some parts of the ribs without subjecting them to a process of decalcification The venous system was congested and there was passive congestion of the *parenchymatous* organs

On reviewing the results of these observations *i e* the four cases just described one common characteristic emerges in each case the heart is about double the normal weight relative to the weight of the body and in each case the enlargement is unassociated with any other abnormality of an anatomical nature in the vascular system As regards the hypertrophy itself it is to be noted that while the right side and interventricular septum participate in a greater degree there is also in every case hypertrophy of the left ventricle The associated anatomical abnormality is in every case that of a *part of the respiratory mechanism* the lungs the chest wall or both The facts then which present themselves for correlation are these

1 General hypertrophy of the heart in an otherwise normal vascular system with relatively greater increase in size of the right side ending in cardiac failure

2 Collapse of the *pulmonary tissue and deformity of the chest wall*

The heart of the healthy subject maintains a size which bears a definite relation to the size and weight of the individual and which is independent of the amount of bodily exertion within very wide limits The heart of a man who pursues a sedentary occupation is no smaller than that of a man whose occupation involves a moderate amount of physical exertion and the amount of work performed by the organ may be greatly increased without *in any way* prejudicing its efficiency or increasing its *size relative to the* weight of the body This property of adaptability is inherent in the heart and is aided by compensatory variations in pressure throughout the vascular system regulated by the vasomotor apparatus The increase in size of skeletal musculature resulting from physical exercise develops *pari passu with an increase in the weight of the heart and the extra work entailed on* the left ventricle is balanced by the aid afforded by greater muscular activity in returning the blood through the venous system The increased thoracic movements in additional muscular activity contribute also to meet the extra

demand which is put upon the circulatory apparatus Moreover the cardiac muscle itself would seem to possess the capacity of immediately adapting itself to an emergency for example Stolnikow has shown that when a ventricle in diastole is artificially filled so as to contain even six times the normal amount of fluid it is able with the next systole to drive out several times the normal amount and in the same way an increased arterial resistance is immediately overcome by the succeeding ventricular contraction The heart thus possesses an enormous power of adaptation and when it shows signs of great hypertrophy and consequent inefficiency such a condition may be regarded as being due to one or more of the following causes

1 Increased work determined either by an increase in the number of beats per minute as in exophthalmic goiter or by increased force demanded against abnormal peripheral resistance as in renal disease or arterio sclerosis

2 Some defect in the pumping apparatus itself such as stenosis of the valvular orifice or valvular defect causing regurgitation

3 Failure of accessory powers of circulation which include the variations in intrathoracic pressure the expanding and collapsing lungs and the movements of the skeletal muscles

When the cases described are viewed in the light of these considerations it is obvious that the causes referred to under the third heading constitute the main factors in the production of the cardiac enlargement at the same time it must be recognized that in each case the pulse rarely was abnormally high although even here the increased pulse rate was probably secondary to the increased respiratory rate or associated with the cyanosis incident to the deficient respiration In any case the factors that are anatomically associated with the hypertrophy are (1) atelectasis (2) rachitic softening with distortion of the thoracic wall

Atelectasis and Cardiac Failure

In the present state of knowledge it is impossible to determine exactly the modification of physiological respiration which is determined by collapse of a considerable portion of the lung Possibly a vasomotor reaction plays a part accommodating the organism to the new conditions or reflex contractions of the muscular rings of the bronchioles may exercise a regulating influence on the disturbed balance of pressure The physical changes are those however which are most easily estimated When a portion of lung collapses there occurs with inspiration distention of the alveoli of the expanding parts at the same time the relatively diminished pressure in the atelectatic portions determines a flow of blood to these parts whereas the compensatory emphysema gives rise to a resistance to the blood flow through the distended portions of the lungs In this way there occurs circulation of a considerable portion of blood through portions of lungs where oxygenation

cannot take place whereas the air circulates through portions where the emphysematous distention of the alveoli hinders the passage of the blood through the capillaries The results of such a condition are

1 Deficient oxygenation of blood with dyspnea and increased cardiac action

2 Increased resistance to the flow of blood through the emphysematous portions of the lungs and the consequent embargo on the right ventricle

3 Stagnation of blood in the collapsed portions of lung with the result that the work of the right ventricle is increased and in addition the heart is deprived of the assistance of the expanding and collapsing lung in furthering the blood flow

Disease of the Chest Wall in Relation to Cardiac Failure

The diseases of the chest wall which are here concerned are

1 Softening of the ribs due to rickets

2 Deformities due to rickets tuberculous caries etc

It is obvious that when rachitic decalcification has produced softening of the bones deformity is also certain to supervene Such processes are most severe between the ages of nine months and two years As a result of loss of elasticity and subsequent deformity collapse of the lung tissue is not infrequent so that the rachitic chest is further embarrassed by the conditions which have been considered in the preceding paragraph

The nature of rachitic deformity and the extent and distribution of a concomitant atelectasis are worthy of notice because they afford a strong confirmation of the conclusion to which Keith has come regarding the mechanism of respiration in man (See also Hoover Respiratory Excursion of the Lung Vol II Chap II) In emphasizing the necessity of recognizing surfaces of direct and of indirect expansion on the lung Keith has rendered a great service to the study of pulmonary diseases in children He has pointed out that the mammalian lung is not equally distensible in all its parts and that it does not expand equally in all directions during inspiration Of the five areas he says which one may distinguish on the surface of the human lung three are in contact with stationary parts of the thoracic wall and therefore cannot be directly expanded These three pulmonary surfaces are

1 The mediastinal in contact with the pericardium and mediastinal structures

2 The dorsal surface lying between the spinal column and the spinal segments of the ribs those parts of the ribs to which the erector spinae muscle is attached

3 The apical surface the pulmonary area lying in contact with Sibson s fascia at the root of the neck

demand which is put upon the circulatory apparatus. Moreover the cardiac muscle itself would seem to possess the capacity of immediately adapting itself to an emergency; for example Stolnikow has shown that when a ventricle in diastole is artificially filled so as to contain even six times the normal amount of fluid it is able with the next systole to drive out several times the normal amount, and in the same way an increased arterial resistance is immediately overcome by the succeeding ventricular contraction. The heart thus possesses an enormous power of adaptation, and when it shows signs of great hypertrophy and consequent inefficiency such a condition may be regarded as being due to one or more of the following causes:

1. Increased work determined either by an increase in the number of beats per minute as in exophthalmic goiter, or by increased force demanded against abnormal peripheral resistance, as in renal disease or arteriosclerosis.
2. Some defect in the pumping apparatus itself, such as stenosis of the valvular orifice or valvular defect causing regurgitation.
3. Failure of accessory powers of circulation, which include the variations in intrathoracic pressure, the expanding and collapsing lungs, and the movements of the skeletal muscles.

When the cases described are viewed in the light of these considerations it is obvious that the causes referred to under the third heading constitute the main factors in the production of the cardiac enlargement; at the same time it must be recognized that in each case the pulse rarely was abnormally high, although even here the increased pulse rate was probably secondary to the increased respiratory rate or associated with the cyanosis incident to the deficient respiration. In any case the factors that are anatomically associated with the hypertrophy are: (1) atelectasis; (2) rachitic softening with distortion of the thoracic wall.

Atelectasis and Cardiac Failure

In the present state of knowledge it is impossible to determine exactly the modification of physiological respiration which is determined by collapse of a considerable portion of the lung. Possibly a vasomotor reaction plays a part in accommodating the organism to the new conditions, or reflex contractions of the muscular rings of the bronchioles may exercise a regulating influence on the disturbed balance of pressure. The physical changes are those, however, which are most easily estimated. When a portion of lung collapses there occurs with inspiration distention of the alveoli of the expanding parts; at the same time the relatively diminished pressure in the atelectatic portions determines a flow of blood to these parts, whereas the compensatory emphysema gives rise to a resistance to the blood flow through the distended portions of the lungs. In this way there occurs circulation of a considerable portion of blood through portions of lungs where oxygenation

can reach the lungs with comparative ease and it is in the lungs that the serious obstacle presents itself The pulmonary circulation is secured by three great forces

1 The driving power of the right ventricle
2 The suction action of the left auricle
3 The pumping action of the expanding and collapsing healthy lung

In the rickety condition under consideration the latter two forces are thrown out of action so that the whole work of propulsion falls on the right side of the heart

The problem however which these cases present is not speculation as to the nature of complicated processes it is rather to formulate what may be termed a correlation of end results and to answer the question Does the circulation suffer from diseased lungs or deficient thoracic movement? Mackenzie emphasizes the importance of examining thoroughly the posterior aspects of the lungs as a guide to prognosis in cardiac disease Extremely suggestive in this connection is his statement (under Onset of Heart Failure with Patients in Bed in chapter on Chronic Diseases of the Heart Vol II Chap XIII) that when the right ventricle is enfeebled the assistance of the respiratory movements becomes necessary When the patient lies in bed *on one side the pressure of the mattress on the ribs restrains* their movement so that the flow of blood through this part of the lung is retarded and edema results This can be shown in the early stages for when the patient breathes deeply the whole of the crepitations may soon disappear A correlation of the evidence in these four cases which have just been described leads definitely to the conclusion that the hypertrophied heart with its broad squat and globular shape is the manifestation of an effort to compensate for the loss of accessory forces of circulation normally present in a healthy expanding lung and thoracic wall Nor are these cases to be regarded as pathological curiosities The variations present are only exaggerated examples of a condition which is probably the determining factor in the issue of a large proportion of the fatal cases of so called broncho pneumonia in underfed children who are brought up in the overcrowded districts of industrial centers In any case the observation of over 1 000 cases of measles whooping cough and diphtheria has led me to the conclu sion that where an intercurrent bronchopneumonia extends over a period of a fortnight the progress of the case has as a rule been complicated by the occurrence of collapse in the case of non recovery the patient has suc cumbed not to the toxic products of the infecting organism nor to the nox ious products of inflammatory decomposition but to the severe mechanical strain which has been put on the heart This strain is due to failure of the accessory pumping assistance of normally expanding lungs and the almost constant occurrence of varying degree of cardiac hypertrophy in such

These three surfaces so far as movements of the chest wall are concerned are relatively stationary The two surfaces of the lung which are directly expanded are the diaphragmatic and ventro lateral or sterno costal these surfaces are the first to expand on inspiration and it is only a re due of the expanding force which is left at the disposal of the more stationary surfaces When one further considers that the lungs of young children are still lobu lated and contain a considerable amount of connective tissue between the expanding areas it will be seen as I pointed out some years ago that the expanding force of inspiration is spent to a considerable extent on tissue of little extensibility There is thus in children an additional claim on the residual expanding force at the disposal of the stationary surfaces of the lungs after expansion of ventro lateral and diaphragmatic surfaces

If these are the conditions in normal respiration how are they modified if the ribs are soft? It is a well recognized fact that the rickety deformity manifests itself most in those parts exposed to mechanical strain The me chanical strain produces a deformity in the first place and in the second place excites further rachitic softening by its irritation thus producing for a time a vicious cycle of events The thoracic distortion is characterized by an in sinking of the chest wall in the upper part of the ventro lateral region Owing to the softening of the ribs the intrathoracic negative pre sure has been able to prevent the expansion of the chest wall over the area of direct expansion The consequence is that the only area of direct expansion is diaphragmatic and clinical examination shows that this is really so In cases of severe rickets the respiratory movements of the upper part of the thorax are scarcely visible whereas the diaphragmatic contractions are relatively increa ed with the result that the abdominal contents are de pressed further than in the normal subject

It must also be obvious that with the depression of the chest wall and the narrowing of the thoracic cavity the surfaces of indirect expansion be come atelectatic In such ca es one finds that the anterior borders of the lungs as well as the posterior parts lying in the hollow between the vertebral column and the ribs are collapsed the centers of the diaphragmatic surfaces of the lower lobes are usually emphysematous only the narrow margin em bedded between the diaphragm and the chest wall being airless

Thus the pathological variation produced by softening of the ribs bears out Keith s contention as to the mechanism of normal respiration But in what way does this variation affect the vascular system? The contrac tions of the diaphragm which are increased in power and rhythm exercise such pressure on the abdominal contents as to secure the flow of blood from the venous cistern to the heart The pressure of collapse of the lung will mean that the negative force which would otherwise be spent in dilating the infundibuli and alveoli will be exerted on the vessels so that the blood

matism is a disease whose histological basis in many cases can be easily identified and whose manifestations in the form of articular fibro muscular and cardiac disease present a fairly constant and typical clinical picture One can but regret that Garrod s classical work published now many years ago should have failed to bear the fruit it promised but it was in accord with the spirit of the times that the solution of the problem be relegated to the laboratory It is not to detract from the real services of bacteriology to suggest that in some respects it has had a paralyzing influence on this particular branch of research Inquisitive minds are set at rest by the publication of a discovery of the organism of rheumatism It is alleged that the organism answers to Koch s postulates and that its inoculation in animals is followed by arthritis endocarditis and chorea But arthritis and endocarditis occur in the human subject as a result of infection by streptococci pneumococci gonococci or meningococci as for chorea its etiology is obscure and though present in some rheumatic subjects it is associated with a variety of conditions with which rheumatism has no connection the idea of experimental chorea in an animal is too ludicrous for discussion

In the absence of a clear conception as to what rheumatism really is and in the absence of an accurate and reliable method of determining which of the so-called "rheumatic manifestations belong to that entity which is characterized by the distinctive histological reaction described in the case of rheumatic myocarditis and fibrositis it is impossible to arrive at a satisfactory understanding of the relationship between rheumatism and heart disease One not infrequently meets with cases of mitral stenosis in which there is no history or evidence of the associated phenomena of rheumatism There is no evidence of arthritis rheumatic nodules chorea or such other complaints as are generally accepted with or without good reason as an expression of a rheumatic diathesis Blindly and perhaps quite correctly such cases are believed to be rheumatic in origin There is so far no evidence to show that mitral stenosis may originate from any other common infections such as pneumonia diphtheria enteric fever gonorrhea or influenza In 400 cases of scarlet fever not a single instance was observed in which a valvular disease comparable with that of rheumatism arose during the period of infection although there were in the series 4 cases of streptococcal endocarditis There were two cases with heart disease on admission to the hospital where the scarlet fever was followed by arthritis which appeared to be rheumatic rather than a result of the scarlet fever In these cases an aggravation of the heart disease occurred

The complexity of the problem cannot be illustrated better than in a brief reference to the association between rheumatism chorea and endocarditis In the course of an inquiry into the associated phenomena in chorea it transpired that while chorea showed some relationship to rheumatism it

cases is very strong evidence in support of that contention Similarly in acute rickets and in subsequent chest deformity there is great liability to collapse of lung tissue more especially in the event of the occurrence of an intercurrent bronchitis Such collapse enhances the disability to which the respiratory mechanism is exposed by the presence of soft rachitic ribs or a restorted and narrow thoracic cavity, the double embargo thus placed on the heart leads to an hypertrophy which can maintain compensation only over a limited period except under the most favorable conditions The period of childhood and even of adolescence in cases of chest deformity may be occasionally survived without any considerable degree of inconvenience and the result of excessive cardiac strain may manifest itself first in adult life

However it is not only in the bronchopneumonia and in the atelectasis of children that these mechanical considerations exercise a determining influence on the circulation One not infrequently meets with cases of deformity of the chest due to spinal caries or to collapse of the lung from old pleurisy in which death has occurred with the signs and symptoms of cardiac failure In these cases the heart is hypertrophied and exhibits the broad quadrilateral shape described above The embargo which has been thrown on the heart through the deprivation of the mechanical assistance of respiratory movements has led to a premature exhaustion of the circulatory system

Rheumatism in Relation to the Circulation

It is comparatively easy to form a clear conception of the biological course of diphtheria or of typhoid fever or of syphilis Every new experience of these diseases renders the conception clearer and more precise With rheumatism the difficulty lies not in the lack of material or experience but partly at least in the loose and inaccurate way in which the term is applied to a variety of conditions which have no recognizable biological relationship to each other

The terms rheumatism and neuritis' are applied indiscriminately to a variety of complaints whose only common feature is the feeling of pain When and how this morass of confused thought and nomenclature is to be cleared up is not a subject for consideration here But it is a remarkable reflection on the state of medicine that a series of complaints so prevalent and fraught with so much discomfort and danger, should have so long escaped the concentrated attention not only of research workers as a whole but of general practitioners who are after all in a much better position to recognize and valuate the symptoms of the protean manifestations of the disease For notwithstanding the abuse of the term and the insistent manner in which it is blamed for pains with which it has nothing to do rheu

firmed by post mortem examination If rheumatism is due to an organism then that organism differs from the other organisms which produce acute febrile diseases in that the subject of infection does not suffer from a disease which runs a definite course and whose prognosis and complications can be explained in relation to the original infection For example in enteric fever the disease runs a definite febrile course subject naturally to great variations both in the character of the fever chart and in its duration but the disease is almost always associated with a bowel lesion and is almost always associated with some form of alimentary symptoms The complications which occur such as hemorrhage peritonitis and bronchitis can be brought into relationship with a perfectly clear conception of the pathological origin and course of the disease With rheumatism on the other hand there is in the conception of its pathology no recognized starting point It is certainly not primarily a joint disease and many of its manifestations occur without fever Some of its most definite signs such as the erythemata leave no recognizable anatomical lesion of a specific character

Another point of contrast between the ordinary bacterial infection and acute rheumatism is that the latter in its several manifestations is amenable in so many instances to treatment with an ordinary drug like salicylate of soda There is no instance of an infection outside of the protozoal group yielding to a drug of this kind If chorea is to be regarded as bearing any relation to rheumatism then that relationship is not a causal one It is highly probable that the rheumatic state is capable of manifesting itself whatever its cause may be in a great variety of ways In this respect it resembles more the character of a syphilitic or tuberculous infection Its manifestations may run concurrently in some cases and in others they may be mutually exclusive The problem of the relationship of rheumatism to chorea does not resolve itself into a question as to whether any such relationship exists but rather as to what the relationship actually is In the cases which we have reviewed a direct relationship of a causal nature between the articular form of rheumatism and chorea certainly did not appear to exist

The Relation of Cardiac Disease to Chorea

Cardiac disease was not a prominent feature in these cases In 8 cases out of the 64 there was definite evidence of valvular disease in an advanced stage In 10 other cases there was a mitral systolic murmur which might have indicated the presence of valvular disease although it is quite possible and indeed probable that in some of these the murmur was functional in origin In 4 cases a mitral systolic murmur was present during the attacks but was absent when the patients were examined subsequently In 3 cases the patients during their first residence in hospital showed no evidence of cardiac disease but on admission for a second time there was evidence of

was much more frequently a motor disorder related in some way to other diseases of the nervous system. It was found apart from rheumatism or apart from the history of any condition accepted as belonging to the group of rheumatic phenomena. It was found with pregnancy, organic brain disease, epilepsy, general paralysis, infantile paralysis, congenital mental deficiency, and with ailments of that ill defined group which is said to exhibit the manifestations of neuropathic proclivity. It was also found unassociated with any other discoverable disturbance, functional or organic.

The Relation of Rheumatism and Chorea

The part played by rheumatism in the symptomatology of the cases under review was a very insignificant one if the term "rheumatism" be restricted to the condition of acute febrile arthritis. Only in 3 cases out of 64 did the chorea develop in immediate association with acute articular rheumatism. In one case the chorea developed a few weeks after the rheumatic fever, and in the other two cases the two conditions were present simultaneously. In 18 cases out of the 64 there was a history of "rheumatism", but it is difficult to estimate the value which should be put on such a history. At any rate, so far as these cases are concerned, the part played by acute articular rheumatism was not a prominent one. It is possible, however, to miss the correct conclusion on this aspect of the subject by taking too restricted a view of the nature of rheumatism itself, for there are no doubt cases of chorea in which rheumatism is present in the form of cardiac disease or rheumatic nodules, and in which the articular form of rheumatism has never been present. At any rate, those cases of cardiac diseases which develop in childhood and in adolescence and progress to a stenosis of the valvular orifices sometimes show no sign of articular disease, and yet show other evidence of rheumatism in the form of nodules, and there is every reason to believe that when a case of chorea is complicated by cardiac disease, that disease is also rheumatic in origin. One must, however, avoid the error of assuming that rheumatic fever is a disease which is comparable with the ordinary acute infections, such as pneumonia and enteric fever. This *is not* the place in which to enter into a discussion on the merits of the respective theories which have been advanced to explain the origin and protean manifestations of rheumatism. It is sufficient to say that no conclusive evidence has so far been adduced in support of the microbic theory. I have examined ten cases of acute rheumatism bacteriologically, examining both the blood and the serous exudates, and I have not succeeded in isolating an organism. In two cases of recurrent rheumatism with advanced heart disease I have isolated a diplo streptococcus which produced arthritis and endocarditis in rabbits, but both cases were low forms of malignant endocarditis superimposed on rheumatic endocarditis, and in each case the diagnosis was con

residence she is almost well In the disappearance of the symptoms the grimacing has remained in a more pronounced fashion than in any of the other choreic movements The mouth condition has from the beginning been treated with chlorate of potash and tincture of myrrh The attacks of petit mal" which were present during the interval between her previous attacks of chorea have completely disappeared since the beginning of the present choreic attack

This woman who was 62 years of age developed a typical attack of chorea She had never had rheumatism and her heart was normal Two of her daughters had had chorea in adolescence but had never had rheumatism either in the articular or in any other form as far as could be made out but one of them was the subject of a well marked mitral stenosis such as in the light of our present knowledge of cardiac disease would be naturally attributed to rheumatism There is here not only the evidence of a deep seated relationship between cardiac disease and chorea but also the indication that it is the hereditary element or neuropathic diathesis which is the most general characteristic of chorea indicating as it does the constitutional proclivity of the tissues of certain families to present the evidence of a certain group of lesions some elements of the group appearing in some members of the family and some in others and even in the case of a single individual different elements appearing at different age Garrod in his well known monograph on rheumatism refers to the occurrence of chorea as a rheumatic manifestation in the following terms

Among the remaining manifestations for rheumatism which are specially common in children chorea holds a prominent place and is often associated with endocarditis in cases in which the joints escape entirely Without entering here upon the difficult question of the relation of chorea to rheumatism the discussion of which is reserved for a later chapter I may express my belief that the endocarditis which in so many instances attends chorea affords evidence that in such cases the nervous symptoms are of rheumatic origin I have more than once witnessed the development of subcutaneous nodules in association with chorea and endocarditis in cases in which there was no evidence of past or present articular troubles and I believe that such cases afford very valuable evidence of the correctness of the above view

Chorea like endocarditis may be the earliest manifestation of the rheumatic state but more commonly it appears as a later event in the series either in direct association with or as an immediate sequel of more definite rheumatic attacks or in patients who have suffered from articular rheumatism at some earlier period Many rheumatic children exhibit a slight incoordination of movement evidenced by twitching of the facial muscles or by some awkwardness of the hands and arms which is hardly worthy of

cardiac disease The irregularity of the pulse which occurs in some cases does not appear to have any relation to organic disease of the heart In some cases it may be nervous in origin and in others it is related to the respiratory irregularity incident to choreic involvement of the thoracic muscles The peculiarly complex nature of the relationship which exists between chorea and cardiac disease is evidenced in the following case

M M aged 62 years was admitted to the hospital suffering from severe chorea involving the arms legs face and trunk The condition had lasted for a fortnight and was associated with an acute inflammatory condition of the mouth

Previous Health — She was always of a nervous and excitable disposition subject to fits of temper and easily irritated A year previously she had suffered from an acute inflammatory condition of the mouth similar to that which is now present It was supposed to be due to decayed teeth Several teeth were removed and a fortnight after their removal chorea supervened For this she was treated in a hospital and after three months residence she was dismissed comparatively well The choreic movements subsided but in the intervening period between the disappearance of the movements of that attack and the onset of the present attack she had suffered from recurrent attacks of loss of consciousness which according to the story, present all the features of petit mal These attacks latterly came on every alternate day Since the onset of her chorea on the present occasion the attacks of petit mal have ceased She has never had rheumatism

Family History —Of three daughters two have had chorea one of them on two occasions and the other on three occasions This latter is also the subject of a mitral stenosis although neither she nor any other member of the family has had articular rheumatism

Condition on Admission —The choreic movements were very exaggerated but slow and of an athetoid type The grimacing constituted probably the most marked feature in the whole picture She was emotional and it was difficult to concentrate her attention The tendon reflexes were exaggerated There was no anesthesia of the skin The mucous membrane of the tongue cheeks and gums was swollen and in places edematous There were small ulcers on the gums The mouth was evidently in a very painful condition Her heart was normal There was no other evidence of disease

Condition during Residence —The treatment during the first week of residence consisted in the administration of chloral and paraldehyde and although sleep was induced especially by the paraldehyde the movements during the waking periods were not much diminished In the second week of residence these sedatives were discontinued and she was given 10 grains (0 65 gm) of aspirin four hourly and from the time when the aspirin was commenced her condition began to improve till now at the end of six weeks

which the whole subject of rheumatism stands and of the clamant need for a simple systematic and thorough investigation This must be carried out on lines which may determine the exact province within which a single causal agency may be operative as an etiological factor Only in this way will it be possible to include or exclude those extraneous complaints which by use and wont and by abuse of nomenclature have found their way into the category of rheumatism This is eminently a field for research on the lines and principles prescribed by Sir James Mackenzie in his recent publication It is essentially the business as it is the exclusive opportunity of the general practitioner to observe the earliest subjective and objective manifestation to watch its progress and varied expressions over years to appreciate the importance or lack of importance of the factors of heredity and consanguinity and to assess at its proper value the significance of the evidence of intermittent predisposing or mutually exclusive ailments

As a necessary adjunct and indispensable corrective to clinical observation and interpretation the cooperation of the pathologist must be enlisted The typical histological reaction in the rheumatic heart and in fibromyositis has been referred to already In chronic cases it may be and often is equivocal but in recent cases it is as distinctive and as characteristic as are the lesions of tuberculosis and syphilis for their respective infections Much may be expected from the contributions of bacteriology and pathological chemistry If an organism be the causal agent then the histological basis suggests a microbe of a higher order than the bacteria and related to the tuberculosis or syphilis or malaria group and this suggestion appears more feasible in view of the frequent response to salicylates Many of the phenomena suggest the presence of toxic agencies without the immediate presence of microbes this applies more particularly to endocarditis and the situation and character of the muscular and fibro muscular lesions are not incompatible with a process of perverted metabolism of the muscle substance

Whether the heart is affected by a poison produced by an organism localized in the region of the lesion as in syphilis or whether it is affected by the toxins of an organism localized elsewhere as in diphtheria or whether the inflammation occurs from a poison elaborated by metabolic perversion in the muscle as shown here and independent of microbic influence these are questions for whose answer we look to the chemist and bacteriologist who work in intelligent cooperation with the clinician

The Relation of Rheumatism to Heart Disease

Despite the somewhat nebulous notions which surround the problem of rheumatism one is justified in the present state of knowledge in assuming that such valvular lesions as are not of syphilitic or pyogenic origin may be attributed to that process or disturbance which lies at the root of these

the name of chorea and which may escape notice unless carefully looked for and between such trifling symptoms and the most pronounced form of St Vitus dance every grade is met with "

The Relation of Rheumatism to Arthritis

There is no form of joint disease which by itself is clinically characteristic of acute rheumatism Acute gonorrheal synovitis of the knee joint may exhibit the same extensive appearances as acute rheumatic arthritis the cytological examination of the exudate reveals no difference although the gonococcus is easily cultivated from the former while the latter is sterile so far as present methods can show Yet there is something in the appearance of the patient in the odor of the exhalation from the skin and in the manner in which the inflammation moves from joint to joint which constitutes a special feature of rheumatic disease the response to salicylate of soda is moreover, a test of some differential importance There is however a form of arthritis associated with organic heart disease in which the salicylates produce little or no effect either on the joints or on the temperature These are cases in which the smaller joints especially those of the hands are involved There is considerable pain, tenderness and interference with free movement and the fever is irregular and seldom high The condition may last for months and is most refractory to treatment and in view of this and of the other distinguishing features referred to the question may quite legitimately be raised whether in such cases one is dealing with a disease quite distinct in its etiology from that of which the ordinary acute articular synovitis is the outstanding expression The presence of heart disease in both cases is not of itself conclusive proof of a common etiological basis Information should be obtained to see whether on the whole the more indolent and refractory type is not more common in patients of a greater age The presence of associated phenomena common to the two types such as rheumatic nodules should be looked for One should not be content with the presence of tender spots which suggest nodules but the nodules should be excised a very simple procedure under a local anesthetic and the histological character determined before accepting evidence of their presence The therapeutic reaction of salicylates is not of much value The variability of syphilis in its reaction to mercury and the contrast between syphilitic meningitis and general paralysis in their response to salvarsan prove how misleading the therapeutic test may be It has not been our intention to attempt to give a systematic review of the manifestations of rheumatism although this would be the natural and necessary introduction to a study of rheumatism of the heart Rather have we found such a review in the present state of knowledge to be impossible The fragmentary and patchy character of our observations constitutes a reflection of the unsatisfactory position in

it is equally characteristic of rheumatic myocarditis to come to a temporary standstill but to be subject to recurrences at longer or shorter intervals The acute stage may be complicated by acute dilatation due to exertion by the freeing of excretions from the valves and the occurrence of embolic infarction by the onset of pericarditis with effusion and the hampering of the cardiac function or by vasomotor reflexes exercising a prejudicial influence on the peripheral circulation Occasionally it is found that the regulatory apparatus in the heart itself is involved in the infiltration process and all stages of disordered rhythm from missed beats to heart block may be met with The tendency however in the great majority of cases is to an abatement of the acute process leaving the heart in a damaged condition which varies from a slight impairment giving rise to little disability on the one hand to an impairment which may be so great as to lead to a permanent inability to respond to the more strenuous demands of life

Treatment of the Circulatory Disturbances of Rheumatism

The treatment of the cardiac complications of rheumatism consists in the first place in the treatment of the rheumatic state Salicylates and aspirin must be employed in the febrile stage although the administration of those drugs does not necessarily prevent the later appearance of cardiac complications It may be however that if these drugs were employed to advantage for a sufficiently long period during and after the febrile stage the possibility of cardiac complication might be diminished It is advisable to employ diuretics in addition to antipyretics Care should be taken in the regulation of diet and of alimentary excretion

Most important of all is strict injunction regarding complete rest The patient should on no account be allowed to leave bed Emotional excitement of every kind should be avoided not only during the progressive stage of the disease but for months after the process has ceased Where subjective symptoms are a feature of the complication counter irritation should be applied over the cardiac region and this may take the form of a blister which should be kept open for a week at least with savine ointment (Unguentum staphisagriae of the British pharmacopoeia) Instead of a blister an ice bag may be employed or alternative applications of heat and cold are frequently found to give relief

In the period of convalescence the progress from the horizontal posture should be gradual The patient should be allowed to sit up and the effect of the change of posture noted Where the pulse is still rapid and small the change in posture should be made with great care In getting out of bed and in walking the reaction of the circulation to increasing exertion should be carefully observed Only after some time should walking on an incline be undertaken When the period of convalescence and exercise in the open air

allied conditions which are accepted as rheumatic But it has been emphasized that the heart wall is also affected in the rheumatic states and to a degree or in a manner which initially at least is more serious than early involvement of the endothelium Death may occur early in the course of acute rheumatism where there is evidence of circulatory failure which cannot be explained by valvular defect but where the interstitial and subendothelial layers of the heart constitute the main seat of reaction and where the fatal issue may be attributed to an involvement of the cardio regulatory or vasomotor system As a matter of fact the great majority of cases of rheumatic myocarditis run a prolonged course Myocarditis endocarditis and pericarditis may occur and recur over a period of years until the signs and symptoms of chronic heart disease have become established The nature and solution of the problems which arise at this late stage are dealt with elsewhere

It is estimated that the heart is affected in 20 to 30 per cent of all cases of rheumatic arthritis It is impossible to determine accurately in what proportion and what relative degree the pericardium endocardium or muscle is involved Generally speaking the cardiac complications are more frequent and more severe in childhood and adolescence than in the later years of life It is more than probable that the myocardium is involved in every case and it is certain that the pericardium is much less frequently affected than the endocardium The first evidence of cardiac involvement may appear in the second week of the disease although as a rule the first symptoms appear at a later date and may even exhibit themselves in the post febrile stage and after the patient has been allowed out of bed The first symptom is usually palpitation and a stabbing pain over the heart or a feeling of tightness or oppression in the left breast Sometimes the symptoms remind one of angina pectoris On the other hand the complaint may arise after walking or slight exertion and it may take the form of feelings of giddiness and pallor In other cases subjective symptoms are absent and abnormality of the heart is first detected on physical examination The pulse may be rapid and soft and occasionally irregular The heart may be dilated both to the right and to the left and a mitral murmur may be present Sudden exertion may give rise to breathlessness and cyanosis On the other hand there may be weakness pallor rapidity of the pulse and the other signs and symptoms which one associates with the sudden onset of cardiac complications in diphtheria These cases are very infrequent but very serious The aortic valves may be involved It is impossible to determine the extent to which the myocardium and mitral valves respectively are affected but it may be taken for granted that where dilatation is present the heart muscle itself is involved in the rheumatic process While it is characteristic of diphtheritic myocarditis to proceed within a limited period to an issue one way or another

fluence on the vasomotor apparatus or which may be looked upon as has already been suggested as reflex phenomena of the nature of shock

Symptoms and Signs of Circulatory Disturbance in Diphtheria

These may be varied and in the initial stages may give no indication of the seriousness of the complication On the subjective side there may be little or no evidence of disease Feelings of tiredness and oppression over the heart may be the only complaint occasionally there may be something approaching an anginal attack and there may be complaint of pain in the region of the liver Loss of appetite apathy and listlessness may come on with suddenness and this may be associated with a sudden striking pallor If in addition to these signs and symptoms there be a slight arrhythmia or extrasystoles or an increase in the rate of the pulse accompanied by lowering of the tension there may be little doubt that the heart has become involved If these phenomena be associated with vomiting not only is the diagnosis assured but the outlook may be regarded as more or less serious Not infrequently a palatal paralysis in the second or third week is followed by a state of apathy and listlessness on the one hand or of restlessness and agitation on the other The patient is pale and vomiting is persistent the pulse is either very rapid and feeble or very slow there is no cyanosis and no edema the liver is enlarged and pain is felt in pressing over it there may be a trace of albumin in the urine This state is indicative of the most serious form of cardiac complication and not infrequently the symptoms remain without abatement for a few days and end in death Less frequently there are one or more intermissions with recurrences and it is only very occasionally that recovery takes place Edema and cyanosis are extremely rare and it is only in the event of an associated nephritis that there is much albumin in the urine The liver on the other hand is almost always enlarged The interference with cardiac rhythm has been the subject of investigation on the part of those who are particularly interested in the pathological changes in the cardiac muscle which induce the various forms of irregularity In an acute degenerative process like diptheritic myocarditis it is impossible to establish a definite basis between alterations in structure and abnormalities in functional activity Heart complications may be associated with extensive degeneration of the musculature where there is only comparatively slight involvement of the auriculoventricular muscle bundle It is practically certain that there are no cases on record where the bundle is involved to the exclusion of the rest of the heart The profound vasomotor disturbances which are almost invariably associated with diphtheritic myocarditis cannot be left out of account in the estimation of the factors which predispose to the various forms of cardiac irregularity Nor can one leave out of account the

is reached altitudes over 1 000 feet should be avoided Not infrequently one finds it necessary to treat a condition of anemia following the complication and this is best done with arsenic and iron Where nervousness is a feature of the early or late stages of the complication the most useful sedatives are the bromide of ammonium and liquid extract of ergot Digitalis and strophanthus and the nitrites and similar drugs employed in the more chronic forms of heart disease are probably harmful in the acute phase of rheumatic carditis Prophylactic measures may be taken in two directions In the first place the patient should be warned to avoid conditions which are supposed to predispose to a recurrence of rheumatism In the second place advice should be given in regard to the disability which has already been incurred The extent to which physical and mental exertion should be incurred or avoided should be carefully prescribed and this should be done in such a manner as not to prejudice the confidence and outlook of the patient Not the least serious disability in many cardiac cases of organic origin is the neurasthenic state which probably originates in the presentation of too doleful a view of the condition

Diphtheria in Relation to the Circulation

There is no infection whose toxins exhibit a predilection for the cardiac muscle in the same degree as those of diphtheria It is estimated that ten to twenty per cent of all cases of diphtheria which come under medical care show signs and symptoms of this complication So far as the period of incidence is concerned it is most frequent in the second and third week but it occurs occasionally in the first week and perhaps least frequently though not least seriously during convalescence and from four to eight weeks after the initial symptoms of infection

The character and varieties of anatomical changes in the cardiac structure have already been dealt with It is impossible to correlate the differences in anatomical degeneration with the variations in clinical phenomena This of course is due to the fact that in conditions of cardiac weakness the circulatory apparatus reacts as a whole and different states and stages of degeneration may present the same type of clinical phenomena Generally speaking the complications which occur in the first week are associated with parenchymatous degeneration of the muscle while those of the second and third week are associated with changes of an interstitial character in addition to those which affect the muscle fiber The complications of convalescence are usually associated with interstitial reaction It should be borne in mind however that the clinical phenomena depend not only upon weakness of the cardiac muscle but also upon profound vasomotor disturbances which may be interpreted either as the direct result of toxic in

patients of course suffer through life from a muscular defect But whereas in rheumatism chronic cardiac disability with endocarditis as the most frequent sequela is often found in the case of diphtheria myocardial disability is the exception and endocarditis does not occur

Basis of Clinical Manifestations of Circulatory Disturbance

It has already been emphasized that it is impossible to correlate the various clinical manifestations with the variety character and degree of the structural alterations in the heart It is important however to recognize that the clinical phenomena arise from two sources in the first place from the weakness of the heart itself and in the second place from the disturbances of the vasomotor apparatus

The disturbances which are due to changes in the heart arise both from destruction of the contractile substance and probably also from the irritating influence of the inflammatory reaction on the intracardiac regulatory apparatus both muscular and nervous Dilatation and mitral incompetence may be due to degeneration of the muscle substance as well as to interference with muscular tonus The pallor apathy frequent restlessness and the enlargement of the liver are ascribed to vasomotor disorders associated with a disturbance of the normal distribution of the blood in the body There is probably an anemia of the brain as well as an anemia of the skin determined by the abnormal flow of blood to the abdominal viscera The possibility of this aspect of the complication being due to shock has already been referred to Whether or not a vagal paralysis is a contributory factor has not been definitely ascertained in spite of the fact that anatomical descriptions have been published which would indicate the possibility of this being the case Care must also be taken of the secondary complications incident to paralysis bronchopneumonia aspiration pneumonia and nephritis

Treatment of Circulatory Disturbance in Diphtheria

It is an open question whether the serum treatment of diphtheria tends to eliminate the possibility of cardiac affection The probability is that the early complications at any rate might be avoided by energetic treatment and it is almost certain that the earlier the treatment is undertaken the less likely are these complications to ensue There can be no doubt that the amount of serum indicated by experimental test is not large enough to combat the more serious form of infection that is to say the amount of serum sufficient to neutralize experimentally a lethal dose of diphtheria toxin is not sufficient to produce the therapeutic effect of much larger doses More severe types of diphtheria ought to be treated with at least 20 000 30 000 or 40 000 immunity units in two or three doses It is an open

extra circulatory factors which may ultimately exercise a determining influence on the adaptability of the circulatory apparatus Palatal paralysis interferes with deglutition more especially when vomiting occurs There may be paralysis of the diaphragm associated with bronchopneumonia and the influence of all these contingencies undoubtedly contributes to a fatal issue

It is estimated that thirty per cent of the cases of diphtheria with cardiac complications die Death may ensue in various ways In the first place it may occur with no premonitory evidence of disability The patient who up to the time of death has appeared perfectly well may collapse and die suddenly after slight exertion Very accurate attention to the progress of the disease might however in such instances lead to the detection of apparently insignificant signs such as occasional irregularities tenderness of reflex origin in some parts of the left thorax or diminution of urine In the second place the onset of the illness may be gradual the pulse may become smaller and more rapid and may then become extremely slow The patient may be apathetic or restless and agitated and in a few days or in a few weeks at the outside death occurs In the third place there may be recurrent attacks of collapse with precordial anxiety dilatation of the heart and liver swelling and this may be followed by a remission during which time the patient is perfectly well for a few days This again may be followed by one or two recurrences terminating in death

In the cases which recover there is also considerable variation in the clinical picture In the first place there may be a complaint of slight weakness with no change in the pulse rate or tension and there may be a slight mitral insufficiency which can be readily overlooked In the second place there may be continuous or increasing weakness lasting from four to eight weeks followed by gradual recovery In the third place there may be some symptoms for two or three weeks and the patient may get out of bed then gradually become worse and after a further period of rest may recover In the fourth place more severe forms which usually indicate a fatal issue may with careful attention and rest pass from a period of great disability with occasional vomiting collapse and all the other features of serious complications and may ultimately recover As a rule the patients who recover make a good and lasting recovery There is a small residue in which weakness slight cardiac dilatation with mitral defect and arrhythmia in the form of extra systoles are present for months or years and may in fact last a life time It should be noted however that diphtheria does not as a rule produce the chronic cardiac weakness which is so characteristic of rheumatic myocarditis nor is it associated with an organic defect of the valvular apparatus In a very few cases there is permanent destruction of the muscle fiber as a result of early parenchymatous change and these

perivascular lymphatics In the chancre the lymphatics are dilated and contain round cells The walls of the veins and arteries are infiltrated and later on the endothelium of the arteries proliferates with still later narrowing of their lumina The perivascular lymphatics which drain the ulcer to the nearest glands become hard and cord like and the glands themselves take on the well known indolent induration which when mixed *infection is present may lead to softening It is in the clear bloodless* sero lymph pressed from the indurated base of the chancre or from the base of the papular syphilide that the spirochaetes can be most readily demonstrated They may also be demonstrated in the clear juice of the indurated glands which drain the site of infection Of low virulence and confined to spaces in which movements of the lymph are slow the organism gradually reaches the thoracic duct through the iliac lymphatics In the very early stages they may reach the blood stream but they do not survive in sufficient numbers to provoke a general reaction It is only when they gain access in large numbers through the thoracic duct to the venous circulation that their general distribution determines an embolic spread which manifests itself in cutaneous lesions Even this eventuality may be delayed or suppressed by the anti syphilitic action of the gaseous content of the lungs and pulmonary *blood which is known to be* inimical to the life of the spirochaete Once settled in embolic form in peripheral sites in the papillary layer of the skin the development of reaction proceeds again in the perivascular lymph spaces as it did in the original chancre Certain tissues of the body exhibit a predilection for the spirochaete harboring it and allowing it to manifest its pathological characteristics Chief among these is the epidermal tissue of the skin and mucous membrane of the mouth and throat and second in pathological affinity comes the central nervous system which is developmentally related to the skin It is during this period of combat with the blood the period between the development of the chancre and the appearance of the rash that the prodromal symptoms of the secondary stage are present Headache malaise generalized pains and occasional fever are the subjective expressions of the reactions which occur prior to the appearance of the sore throat and the exanthem Whether these later symptoms appear and how they appear depend upon individual properties of the host and possibly in some degree also on variations in the infective agent

It is thus seen that in the early stages of the disease the circulatory system is not only the vehicle but the site of infective reaction The lymphatic and hemic circulations are concerned in the process and it is in the lymphatic transformations that the most important diagnostic reactions are discernible The swelling and induration of the subcutaneous lymphatic nodules constitute one of the most important signs of the presence and

question whether in the case of later cardiac complications the repetition of serum is beneficial There is always the possibility in the case of such repetition that anaphylactic shock may occur and contribute an extra burden to the circulation sufficient to produce disastrous results Experience has not shown that digitalis strophanthus camphor and other remedies used in cardiac troubles are of use Adrenalin is sometimes advised and here again the influence of adrenalin on the vasomotor system is in some cases so profound as to be attended with danger in patients in which that apparatus is affected Complete rest of body and mind together with careful dietetic and hygienic arrangements comprise the most important aspects of the treatment of these cases Cold applications over the heart often give immediate relief these may be alternated with hot applications Great care must be taken in the convalescent period to regulate the gradual strain which is put upon the circulatory apparatus as the patient returns to health Sufficient emphasis needs to be laid upon the importance of watching every case from day to day for the slightest evidence of any clinical phenomena which may indicate the approach of cardiac involvement

Syphilis in Relation to the Circulation

The dermatologist is always on the outlook for syphilis and the neurologist usually keeps it in view For the dermatologist it presents itself in a form which though varied and often equivocal has been more or less defined by experience and he sees it at a stage in its development when the history and evidence of original infection may render diagnosis comparatively easy The neurologist recognizes it to be the most common cause of organic disease of the nervous system at least in middle life and although its manifestations may be in many cases indefinite or anomalous an examination of the cerebro spinal fluid provides the means whereby the diagnosis may as a rule be placed beyond all doubt On the other hand the symptoms and signs of circulatory syphilis are very infrequent in proportion to the anatomical incidence of the complication and when present rarely indicate the nature of the process This form of the infection is insidious in its onset and progress and may be present for years without giving rise to complaint With the exceptions of aortitis and aortic aneurysm coronary stenosis or cerebral endarteritis which is usually a mistaken diagnosis for meningitis the specific character of syphilis of the circulatory system usually evades the recognition of the clinician although from the very nature of its pathological character and course the infection is more intimately associated with the circulatory system than with any other system of the body The primary lesion manifests itself in the reaction of perivascular tissue and the organisms spread from the source of infection in the

rise to these aortic changes which are the prelude to aneurysm and syphilitic disease of the heart

Coming to the actual diseases of the circulatory system whose origin is clinically attributed to syphilis there is found that state of confusion which characterizes so many of the medical problems which are concerned with the relation of disordered structure to disordered function Very extensive knowledge exists of the anatomical lesions of the heart and vessels due to syphilis but the clinical conception of syphilis of the circulatory system are for the most part nebulous or inaccurate or both While aortitis and aneurysm of the aorta are recognized as being due to this disease myocardial involvement is regarded as a rarity There is a very general disposition to attribute arterial disease such as atheroma and arteriosclerosis with high blood pressure to specific infection although the most reliable anatomical investigations for example those of Turnbull definitely exclude the justification for such a view On the other hand early cerebral phenomena such as hemiplegia due to meningitis are attributed to endarteritis whereas the arterial condition here is only the vascular accompaniment of the meningitis and the disturbance is not due to lack of blood supply but to the irritation and pressure of exudation

Relation of Syphilis to Arterial Disease

Turnbull s publication on arterial disease is but a short résumé of a very comprehensive and thorough study of the subject It may safely be taken as a most reliable exposition on the problem and its conclusions are confirmed by our own more fragmentary observations which have been carried out by clinical pathological comparisons He divides arterial lesions into (1) hypertrophies (2) degenerations (3) infiltrations and (4) inflammations

1 Dealing with hypertrophies he does not include under this designation the intimal or the adventitial hypertrophies which are of inflammatory origin He expressly confines himself to the well known cardiovascular hypertrophies with high blood pressure which involve both the heart and muscular arteries frequently with incidental renal fibrosis He states that an analysis of the cases does not afford evidence that the incidence of cardiovascular hypertrophy is greater in syphilis than in non syphilitic cases

2 In the degenerations he includes (1) atheroma which comprises all the varieties of primary intimal degeneration and (2) the fatty calcareous and fibrotic degeneration which primarily and essentially involve the media There is no evidence that syphilis is the cause of any one of those types of degeneration and the medial fibrosis can be distinguished from chronic syphilitic medial fibrosis by the absence of inflammatory reaction

progress of the disease in the early stage The glands in the groin in the posterior occipital region and the posterior portion of the sterno mastoid region the submental glands and the epitrochlears are those whose enlargement is of most importance to the clinician In a primary lesion of the hand the epithrochlear will be enlarged in primary affection of the mouth the sub mental gland will be enlarged and it might be advisable in the absence of other determining evidences for example the failure to find spirochaetes in the suspected lesion to excise these glands for spirochaetal and histo logical examination It should be noted that the occipital glands may be enlarged from any irritation of the scalp and that primary infection of the cervix uteri is drained directly into the pelvis and not into the groin

This conception of the secondary embolic spread of the infective agent may account for some of the visceral disturbances which occur in the secon dary stage The occasional incidence of acute nephritis and of encepha litis following both mercurial and salvarsan treatment may be explained on the assumption that in these cases there has been an unusually extensive distribution of organisms by the blood stream and that whereas other viscera have resisted the settlement of infective colonies of spirochaetes these organs have been unable to do so

When as a result of treatment or less frequently as a result of natural resolution the primary and secondary phenomena have disappeared there is no justification for believing that the disease has spent itself In the absence of intensive treatment the virus remains in the lymph spaces and perivascular lymphatics and so far from lying dormant will tend to spread in a clinically latent form This tendency will be proportionate to the absence or inefficiency of treatment A year or even several years after the healing of the initial sore microscopic perivascular nodules may be detected in the site of the chancre Similarly each papule of the papular syphilide is a diminutive chancre with an indurated base distended lym phatics perivascular infiltration and proliferated connective tissue In spite of intensive treatment it disappears slowly and its superficial disap pearance may be deceptive Months after such a rash has disappeared from sight it may be recognized by palpation and even after it is no longer perceptible the presence of the lesion may be determined by histological examination When the rash itself has disappeared its site retains in many instances the residual possibilities of further mischief

The rupial and gummatous infiltrations of the skin which appear in the later stages are no doubt the reaction of dormant microbes whose activity has been only temporarily suspended Apart from the latent nests in these sites the lymphatic spread may continue unnoticed in other channels Without further skin or nervous manifestations the virus may spread slowly along the lymphatics and in later stages of the disease give

Syphilitic Aortitis

From the point of view of the clinician the most important of these degenerations is syphilitic aortitis which not infrequently involves the aortic valves and coronary arteries and which is the most common cause of aortic aneurysm There is considerable doubt as to the period intervening between infection and the commencement of aortitis This is to be expected in a disease whose primary effects on the organism must be obscure It is only when the aortitis has given rise to aortic incompetence or narrowing of the coronary arteries on the one hand or to the pressure symptoms of aneurysm through weakening of the vessel walls on the other that those processes which ultimately lead to symptoms really begin These processes may themselves continue for a considerable period before symptoms make their appearance Aortic incompetence may be made good by ventricular hypertrophy over years more especially in those who pursue a sedentary occupation Narrowing of the coronary arteries may also in such cases be present for long periods without giving rise to the distress which *frequently accompanies this condition Aneurysmal dilatation of the* aorta may exist for years without giving rise to those special symptoms which are the usual source of its discovery As a matter of fact histological examination of the walls of a syphilitic aneurysm shows in the majority of cases that the infection has spent itself or is in a quiescent state Turnbull was able to determine the length of interval between primary infection and death in 32 of his cases The intervals were as follows 7 years 1 case 8 years 2 cases 15 years 2 cases 17 years 1 case 20 years 4 cases 21 years 3 cases 22 years 3 cases 24 years 2 cases 25 years 3 cases 26 years 3 cases 28 years 1 case 30 year 1 case 38 years 1 case 39 years 1 case 40 years 4 cases There is however no indication of the interval which as a rule elapses between infection and the onset of the degenerative changes This interval is presumably shorter than is generally supposed

As to the syphilitic nature of the aortitis in question pathologists are generally agreed Its predilection for the ascending part of the aorta its relative infrequency in the abdominal aorta the characteristic star like cicatrization of the intimal surface the thinning of the media through destruction of elastic tissue and the adventitial infiltration with involvement of the vasa vasorum are as a whole typical anatomical features of the disease The frequent association with other anatomical evidences of syphilis is confirmatory of its nature Not only is syphilitic aortitis the most common complication of the aorta but it is the lesion of acquired syphilis most commonly found in the post mortem room of the general hospital In these cases the Wassermann reaction is positive as a rule

The following is an analysis by Turnbull of his 288 necropsies in which the lesions of acquired syphilis were found Turnbull s observation how

and by the absence of erosion of elastic tissue vessels and also by the absence of adventitial reaction

3 Amyloid degeneration was present in 44 out of 7 924 consecutive necropsies that is in 0 55 per cent It was found in 5 out of 288 examinations in which lesions of acquired syphilis were present that is in 1 73 per cent In 129 cases of chronic pulmonary phthisis in which intestinal tuberculosis was present it was found in 51 thus lardaceous infiltration of the vessels was found in 6 2 per cent of cases of chronic phthisis of this type In complicated and uncomplicated cases of tuberculous spine the percentage was 29 4 and in tuberculous conditions of other bones and joints the percentage was 16 6 It is thus quite clear that although syphilis is a factor in the production of amyloid infiltration its potency as such is not to be compared with that of osseous tuberculosis

4 Blood vessels are not exempt from the infective reactions which involve other structures These reactions may be due on the one hand to the organisms of suppuration such as streptococci or staphylococci or gonococci in which cases the lesions do not present features characteristic of the infective agent or on the other hand the lesions may be of a granulomatous character and in such cases the reaction may be more or less characteristic of the microbe concerned Thus syphilis tuberculosis leprosy, actinomycosis and rheumatism may give rise to arterial changes which though not always distinctive are frequently indicative of the specific type of infection

The spirochaete of syphilis is the most frequent and most important cause of inflammatory degeneration of the blood and lymph vessels In early stages of the disease as has already been pointed out lymph vessels veins and arteries constitute the chief sites of reaction In the latter stages the aorta and the brain arteries are the seats of predilection for specific inflammatory degeneration Vascular involvement in the early stage is part and parcel of the infection itself it is indeed the local expression of the infection in the course of its development but the diseases of the aorta and brain arteries in many cases constitute special degenerations attacking these special structures and comparable with gummatous degenerations of other organisms such as bones testicles or liver

It is impossible within the scope of this review to enter into a consideration of the various inflammatory lesions of blood vessels Suffice it to state that syphilis is the most important factor in inflammatory vascular degeneration and may occur (1) as arteritis in the secondary stage in the brain usually in association with meningitis (2) as phlebitis or periphlebitis and venous thrombosis in the secondary stage (3) as gummatous degeneration of large arteries more particularly of the aorta in the tertiary stage (4) as gummatous phlebitis in the tertiary stage and (5) as gummatous degeneration of the brain arteries in the tertiary stage

Aneurysms exhibiting clinical manifestations were present in 5 of these that is in 11 6 per cent Their sites were 3 in the innominate artery 2 in the right common carotid and 1 in the left subclavian

2 Aortic endocarditis is a frequent sequel or accompaniment of syphilitic aortitis Turnbull found this condition in 45 cases out of his 175 that is in 15 6 per cent Where the aorta is the seat of valvular incompetence in a patient whose cardiac disability commences in middle life and in whose case there is no evidence of the expression of rheumatic diathesis and no history of organic disease of the mitral valve the condition in the great majority of cases may be regarded as syphilitic

3 Where endocarditis is present with aortitis there is not unusually a narrowing of the lumina of the coronary arteries Such narrowing may be sometimes found at the aperture or in the form of a constriction a short distance from the aperture There may be even complete occlusion of one of the coronary arteries This condition gives rise to a nutritional fibrosis of the cardiac muscle which is not so much a source of danger in itself as an indication of the impoverishment of the heart as a whole It is one of the most common causes of sudden death from cardiac failure the terminal phase being probably a state of ventricular fibrillation Diminution in the caliber of the coronary arteries is also recognized as a cause of anginal attacks

4 The cardiac muscle is the seat of syphilitic degeneration far more often than is commonly recognized Large gummata occur seldom but syphilitic inflammatory infiltration and fibrosis can be easily detected by microscopic examination in a large proportion of cases in which aortitis and endocarditis are present Where the inflammatory reaction is recent spirochaetes can be detected it is impossible however to assess the clinical importance of such myocardial changes The histological evidence of the disability is usually found in the perivascular tissue and in the subendocardial connective tissue The amount of muscular destruction cannot be said to be such as to give rise of itself to cardiac weakness or to compensatory hypertrophy as is generally supposed As a matter of fact if one excludes the acute myocarditis of diphtheria and less common myocarditis of enteric fever there are practically no conditions of myocardial degeneration which of themselves account for cardiac weakness In syphilis of the myocardium the aortic valves and coronary arteries are usually involved and it is to this rather than to destruction of muscle that the symptoms are to be attributed In this respect syphilitic myocarditis does not differ essentially from other forms of degeneration of the ventricular myocardium

the presence of syphilitic lesions of the body in 4 per cent of his total cases This of course is a smaller proportion than the general incidence of syphilis in the hospital population would indicate It may be assumed from clinical experience that 10 per cent to 15 per cent of these patients suffer or have suffered from syphilis But from the chronic nature of the disease and also taking into consideration that Turnbull s material includes few cases of nervous syphilis and no cases of congenital syphilis his figures probably represent an incidence which is compatible with the estimate of an infection of 10 per cent to 15 per cent on the whole Even if such a percentage of infection be present in hospital cases at one time or another Turnbull s figures would show that 25 per cent to 30 per cent of these cases developed aortitis and of these cases in which organic lesions were found in a post mortem 60 per cent showed evidence of aortitis

We are not here concerned with the factors which render the thoracic aorta more susceptible to syphilitic inflammatory degeneration than other arteries of the body It is pointed out however in this connection that the aorta has to bear the greatest strain of the extra cardiac circulation and the nearer the heart the greater the strain It should not be over looked however that in many instances the disease stops abruptly at the diaphragm an important fact in distinguishing syphilitic aortitis from atheroma This sharp delimitation of the disease to the thoracic aorta would suggest that some part is played by the variations in intra thoracic pressure These however are points of speculative interest only and our concern is more with the clinical results of aortic disease It carries in its train or is associated in its development with (1) aneurysm (2) endocarditis (3) narrowing of the coronary arteries and (4) myocarditis

1 Aneurysm may of course arise from causes other than syphilis Acute inflammatory endocarditis may spread to the aortic wall and cause a weakening which may give rise to an aneurysm Congenital defect in the development of the aortic arch may occasionally give rise to aneurismal dilatation Advanced atheroma is sometimes also a predisposing factor Syphilis is however the commonest cause and in all the 175 cases of syphilitic aortitis observed by Turnbull there were shallow sulci and pits or diffuse or saccular aneurysms and in 54 of these cases that is in 30 per cent there were aneurysms inducing clinical manifestations including aneurysmal stretching of the commissure

Syphilitic inflammation is the most common cause of aneurysms in other large elastic arteries Such aneurysms arise as a rule in close proximity to the origin of the arteries from the aorta They are rarer however than aortic aneurysms Turnbull found aneurysmal pitting or pouching in all 43 cases of aneurysm of the large arteries which he observed with the exception of a case of arteritis of the second branch of the pulmonary artery

in the walls of vessels of both brain and cord in this case the infection occurred a year and nine months before death

Syphilis of Veins

Attention has already been drawn to the involvement of the venules in the site of primary infection and also of those which lie on the route of infection from its source The venules are also affected in the cutaneous lesions more especially in the papular syphilides and late secondary lesions of the ulcerative type They are also involved in the vascular disturbances associated with recent brain syphilis The pains of a "rheumatic" character *which affect more particularly the lower limbs in the secondary stages are* probably in some cases due to phlebitis Tender cord like thickenings of smaller veins are not infrequently observed and it is not impossible that the persistent tendency to thrombosis after injection of salvarsan in some cases may have its origin in this complication We have observed cases in which such thrombosis occurred on two or three successive occasions and in which there was no question of faulty administration In these cases the patients complained of dull pains in the limbs and of tenderness on pressure over soft parts Phlebitis of the secondary stage is characterized anatomically by polymorphic infiltration of the adventitia and of the intima with occasional thrombosis In many respects it is similar to the tertiary phlebitis which however is frequently associated in addition with periphlebitis of a gummatous character showing a tendency to liquefaction It is of great importance to note that not a few of the so called varicose ulcers of the lower limb are syphilitic in origin and yield readily to anti syphilitic treatment when other measures have proved fruitless

Clinical Manifestations of Syphilis of the Circulatory System

Early Symptoms —Complaints which have reference to the heart are occasionally made by patients in the early and more acute phases of the infection These complaints have not an organic basis exclusively confined to the heart or circulatory apparatus They are indistinguishable from the corresponding phenomena incident to other infections and toxic processes which exercise a debilitating influence on the economy as a whole There appear also in some subjects of syphilis who are of a nervous or hypochondrical disposition disturbances of sensation and disordered feelings which are in the first instance referable to the heart but which are really the expression of emotional instability aggravated by fear of the infection and anxiety as to its consequences These toxic and nervous disabilities tend to disappear with the success of the specific treatment and by the assurance which is an indispensable adjunct to all successful therapy

Phlebitis —Early syphilitic phlebitis which has just been referred to is the involvement of the circulatory system which gives rise to symptoms

Syphilis of Large Muscular Arteries

Syphilis of the large elastic branches of the aorta is much rarer than aortitis and is practically invariably associated with that condition Syphilis of the large muscular arteries is rarer still and in his series of 288 cases of syphilis Turnbull observed it only five times On each occasion aortitis was also present and it was found twice in the celiac arteries once in the superior mesenteric, once in the celiac and superior mesenteric and once in the splenic artery The structural alterations corresponded with those observed in aortitis

Syphilis of the Small Muscular and Elastic Arteries

The smaller arteries are involved in all the structural reactions of syphilis which are proliferative or gummatous in character The arterioles and smaller arteries are usually affected in the neighborhood of gross syphilitic lesions The basal arteries of the brain are however the vessels of moderate size which most frequently exhibit characteristic changes Microscopically they are of a white pearly appearance round and cylindrical and of a firm consistence and distinguishable from atheromatous vessels by the absence of calcification or caseation on their inner surfaces Where caseation is present in these arteries it is on the outer surfaces and this may be determined by incision It may also be remarked that in the case of syphilis especially of recent date the arachnoid is adherent In recent cases microscopic examinations show the pathological process in the arteries to be confined to the adventitia where small masses of lympho cytes are spread in nodular form over the media Occasionally neu trophilic leucocytes and microbic masses may also be observed A few leucocytes may be scattered through the media The intima is usually the seat of extensive proliferative changes This intimal proliferation is usually distinguishable histologically from the intimal hypertrophy or diffused arteriosclerosis with medial hypertrophy and ultimate medial sclerosis accompanied by enlarged heart and high blood pressure In this latter condition the muscular and elastic fibers have a regular arrangement whereas in the granulomatous hypertrophy of the intima in syphilis and in other granulomata the connective tissue and elastic fibers are irregularly dispersed Even where an elastic ring appears on the inner surface of the hypertrophied zone the appearance is quite different from an arterio sclerosis hypertrophy In the cerebral arteries of recent syphilitic in fection spirochaetes have been demonstrated in the vessel walls Cases occurring within six months of infection have been published Benda had a case fifteen months after infection and Strassman has recorded a ca e of meningo encephalo myelitis in which numerous spirochaetes were found

majority 17 out of 31, of Turnbull's cases came to post mortem between twenty and twenty six years after the primary symptoms

Disease of the aorta may of course occur in parts at a distance from the heart and give rise to pressure symptoms of aneurysmal dilatation without directly involving the efficiency of the heart itself When severe cardiac symptoms are present disease of the heart and vessels cannot be distinguished and the organism has already become involved in a complex in which biological adjustment has been strained to the breaking point before the patient seeks advice Premonitory symptoms of a vague character may in some cases herald the stage of irremediable disability Feelings of discomfort and abnormal sensations in the heart region occasional attacks of palpitation indefinite pains and sensations of pressure in the breast with weakness and anxiety may occur in varying degrees of severity over considerable periods prior to the establishment of the well defined symptoms of angina pectoris Mild emotional depression and hypochondriasis may constitute the psychic coloring of the picture although in the presence of such symptoms the possibility of early general paralysis should not be overlooked Even in the absence of a history of syphilis with the foregoing symptoms in a man of thirty to fifty years of age of anemic or cachectic complexion the associated phenomenon of syphilis should be looked for Aortic incompetence without organic complication and the absence of a history and the expression of a rheumatic diathesis are important considerations in a man of that age The conditions of the pupils and deep reflexes should be ascertained and the presence or absence of scars on the throat or base of the tongue or the presence of scars and healed ulcers on the lower extremities should be determined A Wassermann test should be done and a radiological examination of the chest should be made

Even after the syphilitic basis of a cardio-aortic complaint has been determined it is practically impossible for the clinician to interpret the precise nature of the anatomical lesion This difficulty is due to the fact that the structural alterations involve as a rule more than one function of the parts affected an aortitis with aneurysmal dilatation may embarrass breathing by pressure on a bronchus the aortic valves may be incompetent and such incompetence may give rise to symptoms incident to that defect the coronary arteries may be involved with consequent malnutrition of the heart and weakness of the muscle followed by deficiency in the general circulation and anginal attacks due to coronary narrowing

Syphilis of the Myocardium

Gross syphilitic lesions of the myocardium do not occur that is to say there are no diffuse syphilitic degenerations of the myocardium comparable with aortitis or with cerebral syphilis as seen in general paralysis The

based on definite anatomical lesions The condition is comparatively infrequent and may be readily overlooked The pains are generalized and are not acute they are passed over as "neuritic' or rheumatic", like so many other pains of unknown origin They disappear with the subsidence of the acute secondary symptoms Early phlebitis does not give rise to acute inflammatory changes or to liquefaction and we have not observed thrombosis of larger veins in the early stages except as a result of the traumata of venepuncture after salvarsan administration The relation of varicose ulcers to syphilis has already been referred to

Arteritis —Syphilitic arteritis occurs as a rule if not exclusively as part of a more general specific lesion It may be present in practically every syphilitic reaction in chancres secondary nodular gummata and in meningitis It reaches its greatest importance in an etiological sense in the cerebral arteries associated with meningeal changes Here it may of itself exercise an independent influence when occlusion is extreme by interfering with nutrition This is more especially the case when the smaller arteries of the basal nuclei are involved These arteries do not display the free collateral arborization characteristic of the larger branches of the circle of Willis and so obstruction to free flow of blood in them may lead to depression of activity if not to complete destruction of some vital center in the basal structures When the clinical phenomena point to lesions of the cerebrum especially in monoplegia and hemiplegia in the late secondary stage the symptoms are probably due not to occlusion of arteries but to pressure of exudate and in this case early treatment offers a better prospect than in those cases in which basal tissues are affected Reference has already been made as to the variety of ways in which brain syphilis may supervene In the majority of cases the lesions are probably mixed and in practically all the vessels participate The clinician may be satisfied when once the specific character of the disease has been determined to proceed to a more definite diagnosis on clinical data alone is to indulge in guess work which however may be more or less intelligent according to experience

Aortitis —The frequency of syphilitic aortitis has been emphasized It is recognized as of the greatest importance to the pathologist in the elucidation of the structural disintegration leading to death Insidious in its onset vague in its symptomatic expression it develops as a rule in such a manner as to elude even the suspicion of the clinician until the circulatory apparatus has been involved in irreparable damage It is far advanced on its course before it gives rise to aneurysm with its concomitant symptoms of pressure It involves the coronary arteries and the aortic valves before the patient seeks advice and the myocardium degenerates from exhaustion or from failure of nutrition before successful therapy can be adopted It is rarely recognized within the first ten years following infection and the

that complete heart block may occur in advanced cases of atheroma of the aorta where the degenerative processes which show no trace of syphilis spread from the vessel walls to the bundle

Treatment of Circulatory Disturbance of Syphilis

By early and thorough treatment of the infection when it is recognized in its initial stages the occurrence of circulatory complications will usually be avoided These complications may however occur in some cases in which the early phenomena have been ephemeral or in other cases in which the disease has run a latent course In any case in the majority of those conditions irreparable damage involving impairment of function will have resulted before a diagnosis can be made or even before the physician is consulted The therapeutic procedure will depend on the nature of the particular manifestation of syphilis which is presumed to be present

1 Early lymphatic and perivascular infiltrations will disappear in the course of the primary treatment which should include intensive administration of both salvarsan and mercury

2 Cerebral arteritis (or meningitis) of the late secondary stage should be treated with doses of salvarsan beginning with 0 1 gram and gradually increased to 0 4 gram until a total of 3 or 4 grams has been given Mercury should also be given and the result controlled by examination of the blood and cerebrospinal fluid

3 Late cerebral arteritis (chronic meningitis) should be treated by the initial administration of mercury and iodides for a fortnight to be followed by gradually increasing doses of salvarsan the mercury and iodides to be continued meanwhile and the results controlled by examination of the blood and cerebrospinal fluid

4 The greatest precaution must be observed in the treatment of aortitis and its coronary and myocardial complication Preliminary measures of a hygienic and dietetic character must be taken before recourse to the administration of salvarsan The general condition of the patient must be such as to preclude the possibility of circulatory failure incidental to the vasomotor disturbances which occasionally follow salvarsan injection The efficiency of the circulation must be restored to as great an extent as is compatible with the nature of the lesions Iodides and mercury should be administered orally for a period of a fortnight and following this an injection of 0 1 gram of salvarsan may be given This should be repeated every three days for a fortnight when the dose may be increased to 0 2 gram In no case should more than 0 2 gram be given at a time Careful observation should be made to note the possible advent of a vasomotor reaction during the injection This is heralded by a change in the quality of the pulse which takes on a bounding character

nearest approach to such conditions is the diffuse interstitial fibrosis which is sometimes observed in congenital cases In acquired syphilis isolated gummata have been described These may give rise to no symptoms while on the other hand sudden and unexpected death has been attributed to their presence Diffuse granulous proliferation may occasionally be seen in perivascular areas and beneath the endocardium and in these lesions spirochaetes have been demonstrated In late cases this actively proliferating tissue has become fibrosed The muscle fibers are not seriously involved in these perivascular and subendocardial changes

The function of the myocardium is prejudiced to a far greater extent by narrowing of the coronary arteries in aortitis than by any form of direct syphilitic involvement of its structure This is more especially the case where there is aortic incompetence with its concomitant low blood pressure during diastole When the double defect of narrowed coronaries and low blood pressure is present the part of the myocardium supplied by the terminal branches of the longest vessels becomes fibrosed from lack of nutrition and such fibrosis is not so much a source of weakness in itself as an evidence of general impoverishment of the whole organ Syphilis of the heart then when it occurs gives rise to symptoms which are usually due to a complicated lesion or series of lesions which cannot be interpreted on clinical evidence alone and which involve *not only the myocardium* but also the aorta and coronary arteries

There is one condition however in which a localized lesion generally syphilitic gives rise to a definite clinical picture and that is Stokes Adams syndrome or heart block Complete auriculo ventricular dissociation may occur in diphtheria or more rarely in rheumatic fever or perhaps more rarely still in septic endocarditis or influenza But in the absence of these acute infections heart block in a person of advanced years is as a rule due to syphilis The clinical phenomenon depends primarily upon destruction *of the auriculo ventricular bundle as it passes through* the septum fibrosum before its division into the main right and left branches The septum lies immediately beneath the aortic valves and when *syphilitic* aortitis and endocarditis spreads onto the septum the bundle may become involved in the degenerative process In some cases the main bundle itself may escape and either the right or left branch or both may be independently severed after their separation from the main stem The main clinical features of the condition need only be mentioned here slow regular pulse 20 to 40 beats a minute as a rule the auricles beating independently and *more rapidly or in some cases fibrillating* or fluttering and with this slow ventricular rate the occurrence of epileptiform seizures In some cases the block is probably incomplete at first but at this stage it is not likely to come under the notice of the physician It should be noted however

frequent clinically as one would otherwise expect The *infection may find* a site on the base of an old endocarditis where the vascularized tissue of the valves with the wide lymph spaces constitutes a favorable seat for infective reaction

The origin of the disease is as a rule easily discovered Puerperal fever pneumonia furuncle of the skin mastoid disease and septic joints or septic bone lesions indicate the probable source of the series of phenomena in which septic endocarditis finds an expression With regard to the organisms of infection it may be noted that streptococci are most frequently present next in order of importance come pneumococci and gonococci With regard to the streptococcal group it has been noted that the variety composed of long thin chains is the most malignant whereas the short chain variety probably of bowel origin is the least malignant and it is important where the question of malignant endocarditis arises to make a bacteriological examination of the blood

Clinical Phenomena of Acute Infectious Endocarditis

The patients are as a rule healthy and in middle life The initial symptoms frequently do not point to the heart There may be complaint of pains in the joints general weariness difficulty in breathing and occasionally diarrhea In the more chronic types recurrent fever of a doubtful origin progressive anemia and albuminuria constitute the main objective symptoms

In the beginning of the illness the fever may rise gradually and it may be irregular and it is only in the later stages of the more acute types that it is characterized by recurrent rigors and sweatings which are probably an indication of generalized embolic infection There is of course that type of septic endocarditis which in the temperature chart resembles malaria but one should not be misled by the supposition that all or the majority of cases of malignant endocarditis have a temperature curve of that type A period of a week with insignificant and irregular rise in temperature may be followed by recurrent rigors lasting for two or three days and again the temperature may resume an irregular and equivocal character The pulse in the majority of cases follows the temperature curve although in some instances it may be correspondingly more rapid and in others relatively slower

The spleen is usually enlarged and soft and only in long standing cases is it of that hard consistency which renders palpation easy Occasionally the liver is swollen The alimentary canal is sometimes the seat of embolic ulcers and associated with these one finds alimentary disturbances loss of appetite and diarrhea of a dysenteric character

and increases in rapidity, and also by a flushing of the face If any of these phenomena appear injections should be stopped immediately The accessory treatment employed in cardiac syphilis with coronary disease aortic regurgitation or angina should be continued

(5) Varicose ulcers or chronic phlebitis of the latest stages should be treated with salvarsan and mercury in the ordinary way In a case of chronic varicose ulcer excellent results are obtained from the local application of gauze soaked in a 1 in 30 solution of alkalinized salvarsan This may be alternated with the local application of fresh human serum applied in the same way

Acute Infectious Endocarditis

Acute infectious disease of the heart occurs as a complication of generalized septic infection The endocardium and particularly the valvular endocardium is almost exclusively the main seat of the reaction Occasionally there is pericarditis but, although there may be multiple septic emboli in the muscle the lesions are not as a rule such as to produce obvious clinical disturbances except in those cases in which there is an extensive spread from the valves to the adjacent myocardium

On the whole infective endocarditis is a particularly rare occurrence and it is perhaps most frequently seen as a complication of the septicemia incident to some cases of septic puerperal infection where the vascular system is invaded by septic thrombi from the uterine veins It may occur also as a sequela of croupous pneumonia and when this occurs the onset as a rule follows the crisis after an interval of two or three days It may also occur as a complication of septicemia which has originated in a furuncle of the skin It is a rare complication of gonorrhea and of epidemic meningitis

The cardiac lesion varies as a rule with the character of the infecting organism In pneumococcal endocarditis and in streptococcal endocarditis there is usually a shaggy fibrinous deposit composed of large masses of fibrin necrotic material and organisms on the valves In the milder forms of infection the fibrin may be very small in amount and the lesion may be more of the character of a spreading ulcer The aortic valves are more frequently involved than the mitral and the right side of the heart much less frequently involved than the left The ulcerative process may spread into the adjacent portions of the heart rupturing the tendons of the valves involving the bundle of His and extending into the wall of the aorta producing aneurysm and even rupture The opening of the coronary arteries may be involved by the spreading masses of fibrinous exudate Incompetence of the valvular apparatus may occur as a result of rupture of the valves although it has been noted that valvular incompetence is not so

infection and the exclusion of other febrile infectious states such as miliary tuberculosis and typhoid which might present a similar clinical picture must be considered Bacteriological examination of the blood should be made and if negative should be repeated for in the more indolent type of case several examinations may be made with negative results

Embolism —The occurrence of rigors is an indication of the detachment of parts of valvular excrescences and the spread of infection by embolism Embolism is one of the most important indications when it occurs with septic endocarditis it is not clinically however a constant complication The petechial eruptions of the skin have already been referred to as also retinal embolism which has been known to give rise to a purulent panophthalmia Renal inflammation is probably the most frequent form of embolic spread and is associated with hematuria and is to be regarded as a glomerular nephritis due to the embolic spread of bacteria which colonize in the renal glomeruli Embolism of the alimentary tract gives rise to diarrhea and splenic embolism to pain and friction in the splenic region and occasionally to septic peritonitis Cerebral embolism may also occur giving rise to various localizing symptoms hemiplegia monoplegia and affections of vision and hearing Very occasionally the large arteries of the extremities are the seat of embolism followed by purulent inflammation and gangrene

Atypical Cases —Reference has already been made to the difficulty in diagnosing the more indolent forms of septic endocarditis which may run its course for months or even for a year or more One case was observed in which pneumococcal endocarditis following pneumonia passed into a state of abeyance with complete absence of symptoms for six months and this was followed by a recurrence which was fatal Not infrequently one meets with obscure cases of nephritis associated with intermittent temperature and anemia and these after running a course of months are recognized perhaps for the first time on the post mortem table as cases of endocarditis The infecting organism in such cases is usually a short diplococcus or diplostreptococcus of low malignancy and corresponding in its bacteriological features to a form of bowel streptococcus In other cases the main clinical manifestation of obscure septic endocarditis is to be found in an intractable and varying arthritis In these cases bacteriological examination of the joints may give a clue to the nature of the infection and yet the cardiac symptoms may be so equivocal as to leave the question of endocarditis in doubt On the whole the cardiac signs of endocarditis are anything but a reliable indication as to the nature of the

Almost a constant feature of septic endocarditis is the occurrence of an associated nephritis although this complication as a rule passes with out producing the clinical phenomena one would expect This is due to the fact that the nephritis is not of the ordinary type but is of the character of glomerular nephritis and only in exceptional cases so invades the mass of renal tissue and interferes with its function to such an extent as to interfere seriously with elimination Edema and uremia are rare com plications of septic endocarditis Among the most important clinical phenomena are the erythemata or small hemorrhages which occur in the skin These skin hemorrhages are of great diagnostic importance They are more frequently found on the lower extremities than on the upper ex tremities, and are very seldom found on the face and neck They vary in size from one eighth to one fourth inch in diameter The center is dis tinguished from the circumference by a gray necrotic appearance and sometimes by a small abscess Hemorrhages may also be found in the retina and these vary according to the size of the vessel involved

The character of the blood is changed in a manner corresponding to the alterations observed in general septic states Leucocytes are sometimes increased The number and quality of the red blood corpuscles are altered and as the disease progresses anemia dominates the picture

It has already been pointed out that the initial symptoms may begin in the joints They become red and painful and in some instances re semble the condition seen in an acute rheumatic arthritis It is often extremely difficult to distinguish the one condition from the other As a rule however the salicylates have an immediate effect on the rheumatic state whereas they have practically no effect on the septic complication Bacteriological examination is the most certain clue to differentiation Only in rare instances do the joint complications develop to a purulent stage

The mental state of the patient varies from a condition of mild excite ment with a feeling of well being to a condition of restlessness with delu sions and even transient loss of consciousness The characteristic feature of the advanced stage of the disease is that in which the patient although looking very ill admits to a feeling of well being

The foregoing description applies to a state of general septicemia quite apart from a cardiac complication There may be even a very ad vanced state of valvular degeneration with only slight clinical evidence of cardiac disease So much so is this the ca e that advanced cardiac com plications may run to a fatal issue without producing signs or symptoms which would definitely relegate the lesion to the heart All the associated phenomena in a case of this kind should be taken into consideration and carefully weighed The previous history of the patient with regard to

other anti serum such as anti streptococcal serum or anti gonococcal serum This is not the occasion in which to enter into the properties of anti-diphtheritic serum as distinct from other anti era but its obvious influence on certain kinds of non-diphtheritic inflammation of the throat and of gonococcal epididymitis proves that it possesses properties quite independent of those specific properties in virtue of which it is an indispensable adjunct in the treatment of diphtheria

Nephritis which is so frequently present should be treated as part of the general process There is no indication in this respect for diuretic treatment In the case of those patients in whom the period of convalescence has supervened the greatest care must be taken to provide rest for both body and mind The general principle of a gradual return to mental and physical exercise must be kept in view For a con iderable period the strictest injunction must be made in regard to exercise and during thi period every means must be adopted to nourish the body and stimulate *the blood to a return to the healthy state*

Functional Disturbances of the Heart Following Infectious States

Emphasis has already been laid on the fact that it is impossible in every case to correlate circulatory disability with organic or degenerative change in the heart or peripheral circulation Only passing reference may be made to this aspect of the subject here in view of the fact that it is dealt with more fully in another part We have dealt in the preceding paragraphs only with such infections as are frequently complicated by organic disease of the heart Occasionally we find an acute myocarditis in typhoid resembling that found in diphtheria myocarditis has also been described in scarlet fever but these complications are so rare as not to merit especial attention Pneumonia may be complicated as we have seen by septic endocarditis and this applies also to scarlet fever But there is a class of circulatory di turbance characterized by a series of clinical phenomena common to a certain number of infections a functional disorder of the circulation finding an expression in rapidity of the heart palpitation pain over the precordium sleeplessness restlessness all of which symptoms taken together have been designated as irritable heart or disorderly action of the heart Thi condition will most frequently be found as a sequela of some infection such as influenza trench fever malaria dysentery etc *but it may al o be present in nervous patients* in whose history no trace of infection can be found It should be emphasized that this syndrome is also found as an accompaniment of otherwi e latent tuberculo is Whatever it cau e or whatever may be the physiological

disease Even in the case of extensive aortic involvement the only evidence of valvular abnormality may be a functional reflux in the mitral area

Diagnosis in Acute Infectious Endocarditis

The diagnosis must be based on a consideration of the whole clinical phenomena associated in the case As these vary from case to case the conclusion resolves itself into emphasizing the particular outstanding signs and symptoms In one case it may be rigors and in another case it may be anemia and in still another case it may be the emboli which find their seat in various parts of the body Of great importance is the whole course of the case due regard being paid to infectious incidents such as puerperal states pneumonia or skin furuncle in the history of the subject Indispensable to a thorough appreciation of the nature of the trouble is an accurate and repeated bacteriological examination of the blood

Prognosis in Acute Infectious Endocarditis

The great majority of cases terminate after a longer or shorter period in death Where the disease is a complication of acute septic infection they run a course of two to four weeks the issue being determined not exclusively by the cardiac complication but by the toxic effects of the septicemia Only a few cases terminate favorably and it is often the case that the valvular lesion can be determined only after the acute process has subsided

Treatment of Acute Infectious Endocarditis

Treatment resolves itself into attempts to combat the general infection In this respect due regard must be paid to the maintenance of nutrition by the provision of a copious suitable and sustaining dietary On no account with the possible exception of digestive complication should the patient be kept on a milk and fluid dietary So far as possible nitrogenous and carbohydrate foods should be given Strong soups with rice and eggs fresh meat toasted bread and fish should be provided An attempt should be made to vary the dietary so as to make it appetizing to the patient Care should be taken that there be sufficient sleep and rest and camphor may be administered hypodermically with a view to the stimulation of the vasomotor apparatus It is doubtful whether medicinal treatment is of much avail so far as the direct combating of the actual disease is concerned Quinin arsenic and iron may be helpful in their tonic effect on the nervous and digestive systems and in helping the anemia which is almost invariably present It is doubtful whether any of the specific anti sera are of use but for some reason or other anti diphtheritic serum exercises a more profound effect on the human organism than any

CHAPTER X-A

SUBACUTE BACTERIAL ENDOCARDITIS

By EMANUEL LIBMAN AND CHARLES K FRIEDBERG

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sub stratum on which it rests, it constitutes in many cases a very profound disability of the circulation The part played by toxins and the part played by constitutional nervous instability it may be difficult to define but whatever the conditions of the occurrence of this syndrome it is essentially one in which the determining influence of infection must be taken into account

Definition and Classification of Endocarditis

Endocarditis indicates an active inflammatory affection in the valves and sometimes in the inner lining of the cardiac chambers The term has been applied also more loosely to non inflammatory active processes such as degenerative changes or thrombotic deposits which involve the endocardium Endocarditis may involve a normal valve or one which is already the site of an old deformity

Endocarditis may be classified as follows

1 Rheumatic
2 Bacterial
3 Syphilitic
4 Atypical verrucous (Libman Sacks)
5 Nonbacterial thrombotic

Rheumatic endocarditis is not included in the bacterial group although it is believed to be of infectious nature because a specific etiology has not been established and because it has characteristic clinical and pathological features which distinguish it from bacterial endocarditis

Bacterial endocarditis refers only to those cases in which there are found numerous bacteria in spreads or sections made from the surface of the valvular vegetations at postmortem examination The mere finding of the usual causative organisms in the blood stream does not justify the application of this term Bacterial endocarditis usually is superimposed on an old valvular deformity occasionally it may itself initiate or further the deformity

Syphilitic endocarditis is listed as a major group of endocarditis with the reservation that it is seldom a true primary valvular inflammation (gumma) Generally it produces a valvulitis only by extension of an aortitis to the aortic valvular commissures Aortic valvular insufficiency results from the subsequent separation of the commissures and from shortening of the cusps due to tension changes

the valve Any associated clinical picture is so far as known not determined by the endocarditis except for occasional embolization

The term *indeterminate endocarditis* refers to occasional cases which cannot be classified definitely under the above headings The term is employed rarely since the pathology of atypical verrucous endocarditis and nonbacterial endocarditis has been clarified

The *exanthemata* may be complicated by an acute bacterial endocarditis Scarlet fever more often than any of the other contagious diseases is followed by rheumatic endocarditis In addition one of us (I L) has observed in cases of scarlet fever a peculiar form of mitral valvulitis which does not appear to be rheumatic *Tuberculosis of the endocardium* is a rarity

Endocarditis must be differentiated sharply from a valvular defect which usually is the ultimate product of an endocarditis Valvular defects are due to rheumatic inflammation syphilis atherosclerotic and calcific processes and congenital anomalies Occasionally they result from the healing of a bacterial endocarditis and rarely from trauma

CLASSIFICATION OF BACTERIAL ENDOCARDITIS

Bacterial endocarditis is subdivided into acute and subacute bacterial endocarditis As implied in the terminology these subdivisions are based on the duration of the disease the acute form including cases with a course of in general less than six weeks and the subacute cases with a course of more than six weeks This differentiation however is not an arbitrary one except in certain borderline cases The two forms of bacterial endocarditis are as a rule sharply distinguishable both as to their causative agents and as to their clinical and pathological features The acute cases are due almost always to pyogenic organisms while the subacute cases are caused by organisms of relatively low virulence Occasionally subacute bacterial endocarditis results from infection by an organism which usually causes the acute type of the disease while acute bacterial endocarditis occasionally is due to an organism which usually produces the subacute type

Acute bacterial endocarditis most often is secondary to an active local infection which usually is of a surgical nature and readily recognized In this acute form the endocarditis may be a mere incident which is submerged by the prominence of the general and local symptoms of the primary disease On the other hand when the local infection is small or healed the endocarditis alone produces the clinical picture

In cases of subacute bacterial endocarditis the clinical picture is

Atypical verrucous endocarditis (Libman Sacks) is characterized by a peculiar form of nonbacterial vegetation, which may be much larger than that seen in rheumatic endocarditis, and which is very apt to occur on both sides of the valves and on the ventricular and auricular mural endocardium The vegetations may be distinctive in appearance or indistinguishable from those in cases of rheumatic bacterial or nonbacterial thrombotic endocarditis Aschoff bodies are absent The vegetations frequently occur on the right side of the heart and in the pockets of the valves

Peculiar characteristic granular, "hematoxylin stained bodies" (Gross) may be present in the valves, valve pockets and blood vessels The pericardium often reveals a macroscopic adherent pericarditis and characteristic microscopic lesions (Gross) including a granulation tissue containing plasma mononuclear and multi nucleated cells and characteristic proliferating, granulation capillaries (so-called endothelial bud capillaries) but few or no lymphocytes, neutrophilic leucocytes or congested capillaries Vascular lesions may be found in many organs especially in the kidneys The so-called wire loop" lesions of the glomeruli are said to be characteristic, but all would not agree to this since sometimes they are absent from kidneys of these patients and sometimes they occur in other conditions Necrotic and granulomatous lesions of the lymph nodes and spleen have been noted

This form of endocarditis is associated with a characteristic clinical picture (Libman Sacks disease) and usually with acute disseminated lupus erythematosus The clinical picture bears certain resemblances to that of rheumatic fever and of subacute bacterial endocarditis The onset commonly is characterized by arthralgias or arthritis

There is continued fever but blood cultures are negative except for terminal invasions of the blood stream Occasionally white centered petechiæ are observed Not frequently a pericardial rub is audible Albuminuria microscopic hematuria and azotemia are common but the blood pressure usually is not elevated Despite the fever there is usually a leucopenia

Nonbacterial thrombotic endocarditis (Gross and Friedberg) includes most of the cases formerly classified as terminal or cachectic verrucous endocarditis Some of the cases of so called terminal endocarditis prove on careful histological examination to represent a terminal bacterial endocarditis or a fresh terminal rheumatic inflammation The vegetations in the nonbacterial thrombotic group are composed essentially of bland agglutinated blood platelet thrombi which in about 85 per cent of the cases are deposited on deformed usually rheumatic, valves More rarely the vegetations may be deposited on valves which have been affected by arteriosclerosis Monckeberg s sclerosis or atypical verrucous endocarditis (Libman Sacks) or on apparently normal valves Except for the changes of the underlying disease there is little or no inflammatory reaction within

the valve Any associated clinical picture is so far as known not determined by the endocarditis except for occasional embolization

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In cases of subacute bacterial endocarditis the clinical picture is

determined entirely by the endocardial infection The origin of the endocarditis is obscure but it is believed to be secondary to a focal infection which may be latent or active

Terminology

The various terms applied to subacute bacterial endocarditis epitomize the history of our knowledge of this disease Among its numerous synonyms are chronic ulcerative endocarditis chronic malignant endocarditis chronic septic endocarditis chronic infectious endocarditis septic rheumatic endocarditis endocarditis lenta endocardite maligne à forme subaigue

The adjective ulcerative was introduced by Ormerod to distinguish the pathological appearance of the valves and vegetations of this disease from the verrucous type generally caused by rheumatic fever However we know that verrucous vegetations may occur also in bacterial endocarditis The adjective malignant was employed by Osler following Virchow to differentiate this usually fatal endocarditis from the more benign varieties such as the type caused by rheumatic fever But the word malignant leads to confusion with the subject of neoplasms moreover cases of subacute bacterial endocarditis are not invariably fatal The adjectives septic and infectious were substituted when it was recognized that the disease was due to microorganisms but they are less specific than the term bacterial Septic rheumatic endocarditis is a term based on the unproven concept that subacute bacterial endocarditis is merely a virulent or septic form of rheumatic fever rather than a separate disease Finally endocarditis lenta is a term employed by Schottmüller who believes that it is a specific disease due to the single organism the *Streptococcus viridans* This term does not express the known bacterial etiology it fails to indicate that many organisms can produce the disease and the adjective lenta or slow is too indefinite

The general term bacterial endocarditis was introduced because it affords the needed etiological designation When the specific causative organism in a given case is identified its name may be substituted for the term bacterial e g subacute nonhemolytic streptococcus endocarditis acute gonococcus endocarditis or acute streptococcus hemolyticus endocarditis etc Subacute is deemed a better term than chronic to designate the variety of endocarditis the duration of which usually is from a few months to a year and a half or occasionally much longer The substitution of the term chronic for subacute is unwise even in the cases lasting a year or more because these prolonged cases do not differ essen

tially from those lasting less than a year and because the course in the majority is not really chronic in the sense of chronic glomerulonephritis tuberculosis or valvular heart disease

Incidence

The exact incidence of bacterial endocarditis has been obscured by its frequent confusion with rheumatic fever various bacteremias and other diseases As knowledge of its clinical manifestations has become disseminated it is recognized as a common disease and not rare as was believed originally One of us (E L) observed personally at least 1 000 cases from 1899 to 1930 In general subacute bacterial endocarditis follows in frequency the arteriosclerotic hypertensive rheumatic and syphilitic forms of heart disease Its incidence in various localities depends on the incidence of rheumatic heart disease of which usually it is a complication Bacterial endocarditis is a terminal or terminating complication in about 10 to 20 per cent of cases of rheumatic heart disease but in the series of Laws and Levine it was a cause of death in as many as 29 per cent of 148 cases of rheumatic heart disease Subacute bacterial endocarditis occurs much more frequently than acute bacterial endocarditis

SUBACUTE BACTERIAL ENDOCARDITIS

Etiology and Pathogenesis

Causative Organisms

In over 90 per cent of the cases the causative organisms are nonhemolytic streptococci usually of the alpha (viridans) and occasionally of the gamma (anhemolyticus) variety *Streptococcus viridans* is the causative agent which is preeminently identified with the disease But subacute bacterial endocarditis has been produced also by a great variety of other microorganisms including the Pfeiffer bacillus the gonococcus and other members of the genus Neisseria such as *Neisseria sicca* (*Diplococcus pharyngis siccus*) *Neisseria catarrhalis* (*Micrococcus catarrhalis*) *Neisseria flava* (*Micrococcus flavus*) *Diplococcus mucosus* and *Diplococcus crassus* *Micrococcus cinereus* also in this group has not been found to cause subacute bacterial endocarditis These organisms exist mainly as saprophytes in the nasopharynx and like the *Streptococcus viridans* are organisms of low virulence

Subacute bacterial endocarditis may be due also to the *Staphylococcus*

determined entirely by the endocardial infection. The origin of the endocarditis is obscure but it is believed to be secondary to a focal infection which may be latent or active.

TERMINOLOGY

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Experimental Endocarditis

Bacterial endocarditis has been produced experimentally by a variety of organisms and methods As a rule it is produced more readily if a valve is damaged first or if organisms are injected intravenously in association with coarse particles which aid valvular localization It has been caused also by the injection of bacteria after preliminary preparation of the animal by various chemical or immunological measures without direct injury Thus intravenous injections of streptococci and staphylococci have induced successfully a bacterial endocarditis if previously (a) a subcutaneous focus of the same organism was created (b) killed streptococci were repeatedly injected (c) casein pituitrin or lithium carmine was injected intravenously or (d) curvy was produced The presumption is that these forms of preparation altered the immunological response of the valves to bacteria in the blood or caused changes in the subendothelial layer or endothelium whereby bacteria more readily adhered to the valve and set up a bacterial endocarditis However it must be stressed that a bacterial endocarditis may be produced in animals by intravenous injection of bacteria without previous preparation but not as readily

The endocarditis may be produced by multiple injections or even by a single injection of bacteria Occasionally an endocarditis has been produced in animals by simple intravenous injection of the organism isolated from a case of subacute bacterial endocarditis (Libman and Celler Rosenow and others) but similar endocardial vegetations as well as renal lesions have been created by the inoculation of nonhemolytic streptococci obtained from patients with other diseases or by similar organisms isolated from the stools of healthy persons (Horder) The cases of yeast endocarditis mentioned above are examples of accidental human artificial production of the disease

Blood Cultures

In active cases of the disease the causative organism nearly always can be isolated from the blood stream and always observed in spreads from the endocardial vegetations Agonal and postmortem blood cultures usually are unreliable With proper technique positive blood cultures are obtained in 85 per cent to 95 per cent of cases depending in part on the frequency with which cultures are repeated As far back as 1912 one of us (F L) reported 73 positive blood cultures in 75 proven cases of the disease This was before the milder cases were recognized

albus meningococcus corynebacteria (pseudodiphtheria or diphtheroid bacilli) and members of the Brucella group Care must be exercised when organisms having the morphology of diphtheroids are found in stained spreads of vegetations because they may really represent a diphtheroid phase of a nonhemolytic streptococcus Over thirty years ago one of us (E L) found that such organisms in the first subculture or after several transplantations might prove to be non hemolytic streptococci The same caution must be exercised when organisms of diphtheroid character are recovered in blood cultures and elsewhere In 1931 Jensen and Morton drew special attention to this subject They described two strains of organisms which in blood agar cultures appeared as diphtheroids but which were found to be nonhemolytic streptococci when cultivated in dextrose brain broth

Staphylococcus aureus has been reported as a cause of subacute bacterial endocarditis but we have had no confirmatory experience Recently special interest has been attached to cases of subacute bacterial endocarditis due to enterococci These cocci hemolytic and nonhemolytic are characterized by thermostability and other less constant features

In one case (Lamb and Paton) a spirillum was found the *Spirillum surati* *Streptobacillus moniliformis* has been discovered also as a causative organism in several cases of subacute bacterial endocarditis Some of the cases reported as having been caused by a streptothrix or other members of the nocardia group may have been really due to *Streptobacillus moniliformis* as the distinction between these organisms is not clear *Micrococcus tetragenus* also has produced subacute bacterial endocarditis Anaerobic organisms including anaerobic nonhemolytic streptococci and diphtheroid bacilli are occasional causes of the disease Other organisms that have been recovered are erysipelothrix Doederlein bacillus and Bacillus necrophorus (Wilson) Recently Polayes and Joachim reported the case of a morphine addict suffering from subacute bacterial endocarditis due to a monilia This fungus was recovered from the solution of morphine which the patient had injected into his own veins Two other such cases have been observed by Helpern (personal communication)

Subacute bacterial endocarditis may appear in the presence of a mixed infection The most common combination is an endocarditis due to nonhemolytic streptococci with a secondary pneumococcus bacteremia usually secondary to a lobar pneumonia We have observed also a secondary implantation of *Staphylococcus aureus* on valvular vegetations due to nonhemolytic streptococci

positive and negative blood cultures in subacute bacterial endocarditis will be considered under the heading Diagnosis

Baserga and Barbagallo made a comparative study of the results of culture of venous blood and of the material obtained by sternal puncture. They claim that the latter gives a larger number of positive results. We believe in connection with this method that it must be kept in mind that nonhemolytic streptococci may lie dormant for long periods of time in many tissues especially the bone marrow and lymph nodes and be of no pathogenic consequence

Portal of Infection

Usually the site of origin of the endocardial infection is not evident. Clinical observation leads us to the assumption that the portal of infection is as a rule about the teeth or in their roots in the tonsils in the accessory sinuses or in other parts of the upper respiratory tract. The intestinal tract has been suspected also as a portal of entry. Cases of enterococcus endocarditis have suggested such an origin but it should be remembered that enterococci may occur in the nasopharynx as well as in the intestinal and biliary tract. Subacute bacterial endocardititis does not result from a local active purulent infection not even an otitis media. Possible exceptions are the cases which are reported as arising from an infected uterus during the puerperium. However in our experience such cases are either of the acute variety or if subacute are unrelated to puerperal infection and date from before childbirth

Mechanism of Valvular Infection

There has been much difference of opinion on this subject. Three main explanations have been current (1) that the infection takes place by way of capillaries in the valves such capillaries being at times normally present and at other times being dependent upon previous valvular disease (2) that the infection takes place by way of the general blood stream (3) that explanation 2 is correct but that the bacteria are not deposited directly upon the valves but upon small thrombi which have formed on cracks and other irregularities (v Jurgensen Grant)

It is not easy to come to a definite conclusion on this subject but it appears probable that all these mechanisms come into play. At present it is believed that the third mechanism is most common at least as far as subacute bacterial endocarditis is concerned. One must keep in mind that it is probable that clumps of bacteria cause the infection and not

While it is not our purpose here to describe in detail methods of performing blood cultures it is necessary to draw attention to certain important considerations An adequate quantity of blood must be drawn at least 20 c c and a variety of media employed Aerobic and anaerobic cultures should be made Since the organisms may enter the blood stream from the vegetations only intermittently it may be necessary to take repeated blood cultures in order to find the causative organism In suspected cases the blood culture may have to be repeated every two or three days if the first cultures are negative When the patient is experiencing a chill it is desirable to draw blood early during the subsequent rise of temperature In general positive blood cultures are obtained more readily during periods of moderately high fever than when the temperature is normal or only slightly elevated However one of us has seen a patient whose blood culture revealed 200 colonies of *Streptococcus viridans* per c c although his rectal temperature at the time was only 99 2° F Blood cultures should be observed for a minimum of four days but it is preferable to keep them routinely for eight to ten days Sometimes it is advisable to observe the cultures even longer for especially after chemotherapy such as with sulfanilamide or sulfapyridine growth of the organisms may not be discovered until after two or three weeks The blood cultures even may remain completely sterile as long as the patient is under treatment with these drugs while positive cultures are obtained subsequently when they are stopped Recently reported studies (Strauss Lowell and Finland) indicate that by the employment of para amino benzoic acid which inhibits sulfonamide action it will be possible with such a negative result as is obtained to determine whether bacteria are really absent This interesting substance has most effect against sulfanilamide less against sulfapyridine and still less against sulfathiazole Blood cultures similarly may be negative for up to 3 or 4 days after various forms of intravenous therapy whether transfusions or antiseptic chemicals or even saline solution if such therapy is followed by a chill or rise of temperature or both

The number of organisms obtained on blood culture is extremely variable When the organisms are very few in number growth may be obtained only in the flasks (fluid media) As we shall see later a blood culture which is positive only in fluid media must be interpreted with caution Sometimes innumerable colonies are grown on the solid media There is no accurate correlation between the course of the disease and the number of colonies obtained in the blood cultures In any given case the number of colonies grown may remain fairly constant (Schottmuller Libman Weiss and Ottenberg) The significance and interpretation of

virulent pyogenic organisms Furthermore in the absence of previous valvular disease or congenital deformities the valves of the right side of the heart are affected more often than otherwise Such right sided valvular bacterial endocarditis is seen mostly in the acute cases because in the absence of previous deformities infection is determined more by the virulence of the organism than by mechanical factors

Predisposing Factors

1 Previous Valvular Disease — While apparently normal valves may be attacked subacute bacterial endocarditis occurs nearly always on the basis of a previous valvular defect acquired or congenital Usually the acquired valvular defect is secondary to rheumatic fever Uncommonly bacterial vegetations occur on valves deformed by syphilis or arteriosclerosis Subacute bacterial endocarditis may develop in hearts with active or inactive rheumatic endocarditis As a rule it is the patients with valvular defects who have few or no symptoms who are most subject to the disease A specific etiological relationship between rheumatic fever and subacute bacterial endocarditis has been invoked Clawson s suggestion that both diseases are due to the same organism but that rheumatic fever is caused by a more attenuated form of *Streptococcus viridans* is not tenable Swift suggested that rheumatic fever is the result of a streptococcal infection in a patient who is hypersensitive to the organism while subacute bacterial endocarditis occurs when the patient is immune But active rheumatic fever and subacute bacterial endocarditis occur simultaneously in the same patient and even on the same valve Von Glahn and Pappenheimer offered the theory that active rheumatic endocarditis was an essential prerequisite to the occurrence of bacterial endocarditis However definite association of active rheumatic fever could be claimed only in the 40 per cent of cases of subacute bacterial endocarditis in which Aschoff bodies were found Furthermore the theory fails to account for the cases of subacute bacterial endocarditi in persons with previously normal hearts or in those with congenital cardiac anomalies without rheumatic inflammation

Lemann has reported a case in which the disease developed in a mitral valve which had been made insufficient because of infarction of the left posterior papillary muscle due to a coronary artery thrombosis A mitral systolic murmur developed and later subacute bacterial endocarditis eventuated At the postmortem examination the left posterior papillary muscle was found shortened because of scarring and was held down to the scarred wall of the ventricle Two other cases have been reported in

single ones Aside from the difference of expert opinion as to whether capillaries actually exist in normal valves the frequency with which individual valves are affected in subacute bacterial endocarditis seems to deny the importance of valve vessels in the pathogenesis of the disease Thus the tricuspid valve which most often (Gross) contains vessels normally is involved rarely, while the aortic valve which is least likely to have normal vessels is involved very often Furthermore the occurrence of bacterial infection on the mural endocardium which normally is free from vessels indicates the importance of direct implantation of bacteria However it remains possible that in previously inflamed valves which are rich in blood vessels infection may occur by way of these vessels as well as from the general blood stream

The sites of localization of the bacterial endocarditis are determined chiefly by mechanical factors There is evidence that bacteria settle and multiply wherever they are sprayed forcefully on a receptive area The major sites of localization are valves deformed by rheumatic fever chiefly the mitral and aortic The factors concerned may include the greater pressure and the higher oxygen tension in the left cavities of the heart the greater ease of adhesion of bacteria to the irregular surfaces of the deformed cusps and the altered immunologic response of the damaged valves

Even in the absence of an obvious previous inflammatory change or valvular deformity the localization of a bacterial endocarditis may be determined by mechanical impingement of the blood stream Tension and rubbing are very important in the pathogenesis of the disease Thus in hearts with a patent ventricular septum the endocarditis may appear on the endocardium of the lateral wall of the right ventricle opposite the defect through which apparently a stream of the blood containing bacteria is sprayed against the opposite wall In the presence of a coarctation of the aorta the lesion is found below the isthmus In instances of aortic insufficiency with endocardial pockets in the left ventricle below the aortic valve endocarditis often may be found in the vicinity of the pockets presumably in the course of the regurgitant stream Other sites of endocarditis are determined by contact spread and rubbing Of particular interest are such infections of the root of the aorta and of the aortic flap of the mitral valve secondary to vegetations on the aortic valve

Finally there are not infrequent infections of the apparently normal valvular or mural endocardium These are more frequent the more virulent the organism Consequently primary bacterial endocarditis is observed most frequently in the cases of acute bacterial endocarditis due to

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which it appears that a similar mechanism was involved It must be noted that after a coronary artery occlusion subacute bacterial endocarditis may occur in a previously diseased valve just the same as in other patients Recently we observed a patient who had suffered two attacks of coronary occlusion and in whom a subacute bacterial endocarditis occurred on the basis of an old aortic insufficiency

Of special interest is the association of subacute bacterial endocarditis with biscupid aortic valves Lewis and Grant noted that more than 23 per cent of males who reached adult life with this abnormality died of subacute bacterial endocarditis Recently Gross presented evidence that the majority of bicuspid aortic valves are not congenital anomalies but the result of the healing of a rheumatic infection

2 *Congenital Cardiovascular Abnormalities* —Congenital anomalies are next in importance to rheumatic deformities as predisposing factors of bacterial endocarditis Subacute bacterial endocarditis usually affects the left side of the heart because of the great frequency of previous rheumatic valvular disease in the valves of the left side But in the presence of congenital cardiac lesions this disease usually is found on the right side of the heart Of the grosser congenital abnormalities patent ductus arteriosus is associated most often with bacterial vegetations Less commonly bacterial endocarditis occurs in cases with ventricular septal defects coarctation of the aorta and pulmonary stenosis In the presence of some of these congenital lesions the bacterial vegetations may be limited to the intima of the aorta or pulmonary artery These are cases of subacute bacterial arteritis but the clinical picture and course are essentially identical with that of bacterial endocarditis Analogous lesions occur in the presence of an arteriovenous aneurysm usually of traumatic origin and involving most often the iliac or femoral vessels

3 *Physical and Mental Strain* — Because of the tremendous rise in the incidence of bacterial endocarditis toward the end of and following the Great War I physical and mental strain have been invoked as possible predisposing factors The patients affected were almost exclusively men who had seen prolonged active war service in whom previous cardiac defects were uncommon The greater frequency of involvement of the aortic valve in these cases of so called war endocarditis may merely indicate that persons with readily recognized mitral lesions were excluded from war service while those with aortic lesions may have had biscupid valves which could not be recognized clinically and it was the presence of this congenital anomaly and not strain that was the factor predisposing to bacterial endocarditis in these patients

4 *Grippal Infections* —According to histories of patients with

subacute bacterial endocarditis this disease not infrequently is a sequel of an attack of grippe. There is no such clear relationship between subacute bacterial endocarditis and the preceding respiratory infections as there is between rheumatic fever and respiratory infections. In many instances the so called grippal episode probably represents an early manifestation of the endocarditis itself. On the other hand an upper respiratory infection may favor implantation of the bacteria on the valves.

5 Operative Procedures.—Occasionally the symptoms of subacute bacterial endocarditis begin after an operative procedure especially following the extraction of a tooth and less often after tonsillectomy. The nonhemolytic streptococci are the commonest organisms found in infected tonsils and dental apical abscesses and may be thrust into the blood stream by the operation. Okell and Elliott observed that dental extractions were followed by transient bacteremias usually of *Streptococcus viridans* in 75 per cent of patients with septic mouths and even in 34 per cent of persons without obvious oral infection. Such transitory bacteremias while relatively inconsequential in the normal person may set up a bacterial endocarditis in persons with valvular defects which aid localization of the organisms. It should be emphasized however that because of the difficulty of dating the onset of subacute bacterial endocarditis and because of the frequency with which dental extractions are performed often it is not possible to say whether these associations are merely coincidental or causative.

6 Pregnancy and Puerperium.—Subacute bacterial endocarditis may appear to have its onset during pregnancy or shortly after childbirth. As with operations the relationship may be coincidental. On the other hand it is possible that in the presence of pelvic inflammatory disease childbirth may produce a transient bacteremia with consequent subacute bacterial endocarditis in predisposed persons. In our experience gross infection of the uterus during the puerperium may be followed by acute and not subacute bacterial endocarditis. When the latter disease was present the onset nearly always could be referred back to some period before childbirth.

7 Age and Sex.—About two thirds of the cases of subacute bacterial endocarditis occur in the third and fourth decades of life. Less commonly however the disease affects persons at any age of life from early childhood to old age. But like rheumatic fever subacute bacterial endocarditis is found rarely before the age of five. The oldest patient we have seen was seventy four and the youngest a child of four. There is no significant predilection as regards sex but in our experience males are affected somewhat more commonly.

PATHOLOGY OF SUBACUTE BACTERIAL ENDOCARDITIS

Heart

The fundamental feature of the disease is the presence of *bacterial vegetations* on the valves or less often on the parietal endocardium the aorta the pulmonary or other arteries The vegetations may be green yellow pink or red in color and become gray with healing The vegetations differ from those of rheumatic fever in two essential respects which account for the most important clinical difference between the two diseases In the first place the presence in the vegetations of bacteria which are readily washed into the general blood stream gives rise to the bacteremia and toxemia which characterize subacute bacterial endocarditis In the second place the vegetations usually are larger and much more friable than those of rheumatic fever so that particles are readily broken off and disseminated as embolic masses which reach distant parts of the body by way of the blood stream Rarely the vegetations form huge cauliflower masses which are capable of occluding the valvular orifice and sharply reducing the cardiac output

The vegetations usually are situated on the left side of the heart the mitral the aortic or both of these valves being affected in that order of frequency Uncommonly the tricuspid and pulmonic valves are affected also The vegetations on the mitral valve may extend down the chordæ tendineæ to the apex of the papillary muscles (Fig 1) The chordæ may become necrotic and rupture The aortic valvular vegetations frequently spread by contiguity along the ventricular endocardium or by impaction produce an irregularly ulcerated bacterial lesion on the ventricular surface of the anterior mitral cusp (Fig 2) A characteristic worm eaten appearance occasionally is seen on stenotic mitral valves which are affected secondarily by subacute bacterial endocarditis Parietal lesions occur predominantly in the left auricle and in the left ventricle below the aortic cusps and on the papillary muscles The auricular lesion often is superimposed on the characteristic rheumatic auricular lesion When fibrous irregularities are formed as a result of healing this lesion has a characteristic coarse sharkskin appearance (Gross)

Certain pathological complications of the valvular vegetations may lead to clinical symptoms Necrosis of the valve substance may cause the formation of aneurysmal pouches When the valvular destruction is extensive the cusps may be perforated The sinuses of Valsalva occasionally are the seat of aneurysm formation A mycotic aneurysm at the base of the aorta may extend into the pericardial space between the roots

of the aorta and pulmonary artery and produce a hemorrhagic or fibrinous pericarditis or both. Bacterial lesions in the aortic and uncommonly in the tricuspid valve may burrow into the subjacent myocardium of the interventricular septum or into the septum fibrosum. In contrast to the

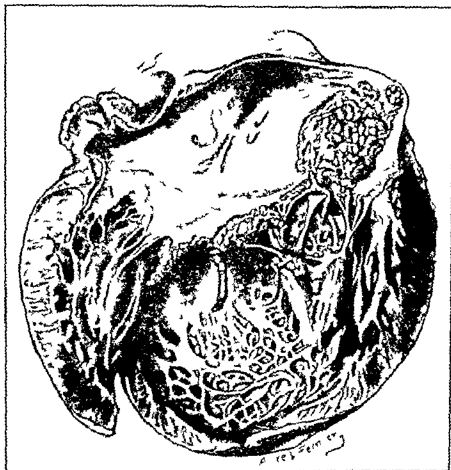


FIG 1 Subacute bacterial endocarditis (nonhemolytic streptococcus), active stage, characteristic location of [illegible] of mitral valve with involvement of chordae tendineae and papillary muscle, extensive involvement of posterior wall [illegible] left auricle

occurrence of this complication in cases of acute bacterial endocarditis they almost never cause interventricular perforation.

Fresh and healed rheumatic vegetations may be present side by side with the bacterial lesions. The valves frequently show the changes caused

Healing is an early and prominent feature as recognized by Osler Bacteria tend to disappear In addition to the inflammatory cells just mentioned the cusp may contain numerous capillaries and fibroblasts As a result of hypercapillarization anastomosing cavernous channels may be formed which produce a distinctive spongy lesion (Gross) Considerable fibroblastic replacement may occur If healing is prolonged there may be calcification of the vegetation whose microscopic structure assumes an appearance resembling necrotic liver cords (liver lime lesion of Gross) The vegetations in different parts of the heart may show varied degrees of healing Healing may occur in some of the lesions while others in the same heart are still in the active bacterial stage These are the so called transitional cases from a pathological standpoint In recurrent cases fresh lesions may be found superimposed on healed ones

The *myocardium* shows a variety of lesions which are rarely as significant as in rheumatic fever unless there are concomitant active rheumatic lesions Frequently there are diffuse or localized collections of lymphocytes and mononuclear cells When localized they form the so called Bracht Wachter lesions which unlike Aschoff lesions have been produced experimentally Also unlike Aschoff lesions they replace the muscle itself instead of lying in the interstitial tissue Occasionally there are diffuse infiltrations of polymorphonuclear cells or localized collections of such cells with or without myocardial necrosis or miliary abscesses Gross suppuration is absent The muscle fibers may show degenerative changes often there are small scars in various stages of healing The small coronary branches show swelling and proliferation of the endothelial cells of capillaries and arterioles arteriolitis or necrosis of the media or adventitial and perivascular cellular infiltrations and scars A large branch of a coronary artery may contain an embolus or reveal a mycotic aneurysm Saphir has stressed the occurrence of small emboli minute infarcts and focal necrosis DeNavasquez found emboli resembling bacterial vegetations in structure in the coronary arterioles of 16 of 20 cases of subacute bacterial endocarditis bacteria were demonstrated histologically in 6 of the 16 cases

In addition to the lesions associated with subacute bacterial endocarditis per se there is usually a variety of alterations chiefly in the interstitial tissue and around the blood vessels alterations which are caused by the associated active or inactive rheumatic heart disease In about 25 to 45 per cent of the cases Aschoff bodies are present They may represent an intercurrent or terminal rheumatic infection rather than one which preceded the bacterial infection An active rheumatic valvulitis

as well as active rheumatic vegetations may be present at the same time and on the same valve as the bacterial lesions

A macroscopic pericarditis is rare except insofar as it is due to a previous or coincident attack of rheumatic fever A fresh fibrinous pericarditis may be due to a concomitant rheumatic inflammation to uremia to an intercurrent lobar pneumonia to subpericardial infarction of the myocardium or penetration of a mycotic aneurysm through the base of the aorta or to mixed infections

Vascular Lesions

Vascular lesions are an essential feature of subacute bacterial endocarditis Two forms may be considered (1) embolism including mycotic aneurysm and (2) arteritis

Embolism affects chiefly the large vessels of the brain but also those of the extremities especially the popliteal and radial arteries and of the internal organs notably the spleen kidneys lungs and intestines Any artery may be affected Embolism produces symptoms by stoppage of the blood supply with secondary infarction or gangrene or occasionally by the production of *mycotic aneurysm* in the wall of the vessel While these aneurysms may occur in almost any vessel they arise particularly at the bifurcations of vessels that lie in the soft tissues The brain the heart and the base of the aorta are sites of such aneurysms which may lead to fatal complications Rupture of these aneurysms is not uncommon and causes serious and fatal hemorrhages Occasionally rupture of an aneurysm leads to the formation of a false aneurysm (Fig 4) or the rupture may occur into a neighboring vein with the production of an arteriovenous aneurysm

Aneurysms may result not only from infected emboli arising in the valvular vegetations but also from bacterial infection of the arterial wall without gross embolization In many cases of perforated mycotic aneurysms there is no visible embolus Apparently the arterial wall is infected most often by the bacteria in the blood stream by way of the vasa vasorum Infection through the intima is another possible mechanism Bacterial arteritis with necrosis and weakening of the wall results in aneurysm but necrosis may lead to rupture without aneurysm formation

Arteritis of the small vessels particularly capillaries and arterioles is being recognized as a common occurrence in this disease These are presumed to be toxic possibly allergic lesions as bacteria are absent Various cutaneous lesions such as the Osler lesions and others to be described later as well as certain of the renal lesions are now considered to be

due probably to inflammation of the walls of the small vessels associated with endothelial hyperplasia and the obliteration of their lumens Intense arteritis necrotizing arteritis without local bacterial infection has been reported in the testicle and in the choroid layer of the eye by Helpern and



Fig 4 Subacute bacterial aortiti (nonhemolytic streptococcus) active stage coarctation of aorta vegetations on aortic wall with ulceration perforation and formation of false aneurysm pulmonary hemorrhages due to leakage through the aneury m

Trubek in a case of subacute gonococcal infection of the pulmonary valve in which numerous gonococci were found

Bacterial infection of a preexisting arteriovenous aneurysm may occur

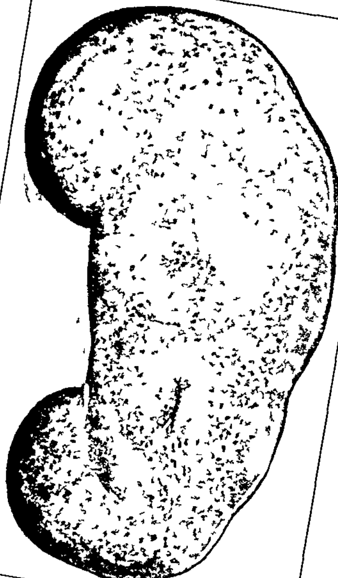


FIG 5 Subacute bacterial en locard t act ve t g characterist c flea bitt n
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in the absence of a concomitant endocarditis or it may be secondary t a bacterial endocarditis The endocardium may be infected after th bacterial arteritis is already present as indicated by the relative size an

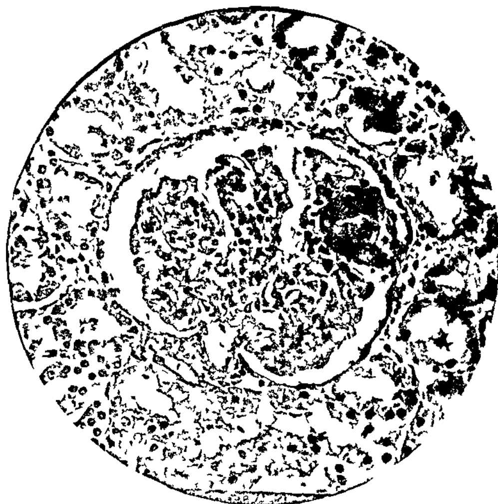


Fig 6 Subacute bacterial endocarditis partial glomerular lesions (Lohlein) early stage of necrosis of part of the glomerulus (From Baehr Jour Exp Med 1912 XV 330)

pathological age of the two lesions The iliac artery and vein and the femoral artery and vein have been affected most often

Thrombophlebitis is rare

Kidney

Three types of renal lesions are encountered (1) the partial glomerular lesions (2) diffuse glomerulonephritis and (3) infarctions

The partial glomerular lesions first described by Lohlein as focal embolic glomerulonephritis are almost specific for the disease having been found in all but 2 of 68 cases studied by Baehr. This lesion has been noted in cases of subacute bacterial endocarditis due to nonhemolytic

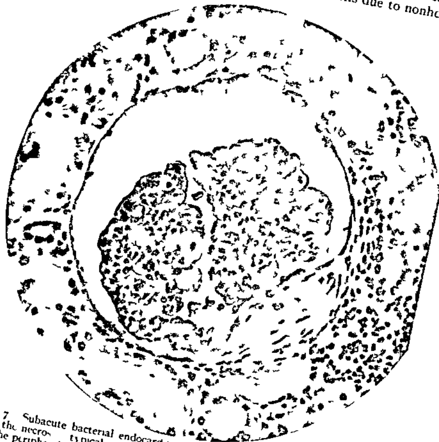


Fig 7 Subacute bacterial endocarditis partial glomerular lesion (Lohlein) final result of the necrosis typical wedge shaped fibrous lesion with epithelium reflected over it from the peripheral layer of Bowman capsule no change within the glomerulus in other portions of the capsule (From Baehr [illegible] 330)

streptococci the Pfeiffer bacillus and other organisms. However in cases of this disease caused by the gonococcus there is either an intracapillary glomerulonephritis or a subacute diffuse glomerulonephritis but no partial glomerular lesion.

Grossly the kidney is dotted with innumerable tiny hemorrhages

producing a characteristic flea bitten appearance (Fig 5) Microscopically the feature of the lesion is the necrosis of only a portion of the glomerular tuft and the presence of a fibrinoid plug in the lumen of the corresponding glomerular branch (Fig 6) The lesion usually has been regarded as being due to emboli but it is probable that local vascular inflammation and closure play a contributory if not dominant rôle in its production The swollen necrotic portion of the glomerulus degenerates becomes hyalinized fibrosed and adherent to the parietal layer of Bowman's capsule which covers it with a reflection of epithelium A characteristic wedge shaped or pyramidal lesion results (Fig 7) Few or numerous glomeruli may be involved In the bacteria free stage the healed hyaline or fibrous form of the lesion is observed

Acute and subacute diffuse glomerulonephritis are far less frequent in the active stage than in the bacteria free stage of subacute bacterial endocarditis In the cases due to the gonococcus or to pyogenic organisms the incidence of subacute glomerulonephritis is high Occasionally both the partial glomerular lesions and diffuse glomerulonephritis are present simultaneously

Infarcts are frequent and may be small or large One or more infarcts may be present They are generally bland but in the cases due to the enterococcus they are reported occasionally as being purulent

Spleen

The spleen usually is enlarged often being of huge size We have twice seen a spleen weighing 800 gm spleens weighing 400 gm or more are not uncommon The gross appearance is that observed in other kinds of general infection acute or subacute splenic tumor but in addition there are usually large and small wedge shaped and irregular infarcts The infarcts are apt to have a yellowish (ochre) color and bevelled borders Perisplenitis is common and may lead to adhesion of the spleen to the diaphragm Occasionally a large infarction appears to form an abscess but bacteria are not so abundant as with true suppuration These abscess like formations are due usually to autolyzing necrotic tissue Rupture of an infarct may occur and may result in intraperitoneal hemorrhage subdiaphragmatic or retroperitoneal suppuration or peritonitis Microscopically the spleen presents the picture of subacute or chronic infectious splenic tumor Amyloidosis has been described a number of times

Other pathological findings will be discussed in connection with the symptoms referable to individual organs

Clinical Features of Subacute Bacterial Endocarditis

Introductory

It is important at the outset to draw attention to certain differences between the general aspects of the symptoms of rheumatic acute bacterial and subacute bacterial endocarditis In rheumatic fever the endocarditis is only one manifestation of a widespread generalized disease The clinical picture may be dominated by symptoms due to involvement of the joints the skin the endocardium the myocardium the pericardium the blood vessels the brain or other organs alone or in combination In acute bacterial endocarditis there is often present an extensive primary lesion such as osteomyelitis puerperal infection lateral sinus thrombosis etc If the primary focus is still active and the endocarditis extensive the clinical picture is due to both If the primary lesion is extensive and the endocarditis slight the picture may be due practically entirely to the primary focus But if the primary lesion is light or already healed the endocarditis plays the whole role

In subacute bacterial endocarditis the symptoms are due to the endocardial involvement or its complications while the primary focus usually is either undeterminable inactive or relatively insignificant The endocardial lesions produce symptoms by way of the associated toxemia and bacteremia because of their effect on the valves and adjacent structures and because the release of particles of the vegetations usually containing bacteria produces embolisms and embolic aneurysms

Mode of Onset and General Course

The onset of the disease usually is insidious As a rule the patient is known to have suffered from a cardiac lesion which has been well compensated He may be up and around long after the disease has begun The first symptoms are variable and often difficult to determine because of their slow development Most often there is lassitude or weakness anorexia and a low grade fever The patient may complain of undue fatigue toward evening and an unwonted desire to go to sleep early Often the beginning of the disease may be dated more accurately from the time of appearance of the latter symptom than from that of the onset of fever The patient may complain of vague and diffuse pains such as occur with a grippal infection This may lead to his temperature being taken and the discovery of an endocarditis

Sometimes the patient first consults the physician because of a loss

of weight A careful review of the patient s history may reveal a respiratory or other febrile infection from which the patient seemed to recover but after which he never returned to a state of good health or complete apyrexia At times the patient suffers an acute rheumatic episode with fever and arthritis which symptoms merge imperceptibly into a complicating bacterial endocarditis The symptoms of the disease may seem to develop insidiously after an operative procedure or after child birth Almost any symptom of the disease may be its first manifestation particularly cardiac weakness urinary symptoms pulmonary symptoms headache vertigo or digestive disturbances

Occasionally there is a sudden onset characterized by a sharp elevation of temperature with or without chills or by evidences of embolism of one of the cerebral visceral or peripheral arteries Thus the onset may occur acutely with hemiplegia local paralysis of an extremity embolism of the retinal artery or sharp pain in the abdomen or lumbar region due to a splenic or renal infarction

The earliest combinations of symptoms are such as to simulate a variety of diseases with which subacute bacterial endocarditis may be confused This is due to the fact that the earliest symptoms either are of a very general nature resembling those caused by numerous other febrile diseases or are determined exclusively by infarction of a single organ thus resembling a host of other diseases affecting that organ Among the combinations of symptoms with which subacute bacterial endocarditis may begin are the following (1) headache general pains malaise weakness and respiratory symptoms like those of influenza (2) fever cough loss of flesh sweats weakness pain in the chest and perhaps hemoptysis as in pulmonary tuberculosis (3) fever and prominent joint pains simulating rheumatic fever (4) fever and diarrhea or fever headache diarrhea and drowsiness similar to the onset of typhoid fever (5) intermittent fever and chills resembling malaria (6) evidences of myocardial disturbance may predominate especially dyspnea palpitation precordial pain and sometimes subcutaneous edema (7) fever and pain in the right hypochondrium may be the first manifestations giving rise to the diagnosis of hepatic suppuration or subphrenic abscess (8) there is a renovesical type of onset with abdominal pain and urinary symptoms with or without hematuria (9) an onset with loss of weight and gastrointestinal symptoms such as vomiting postprandial distress and anorexia may simulate gastric carcinoma (10) the clinical picture of the onset may resemble that of acute appendicitis (11) the initial clinical picture may be that of a basal cerebral hemorrhage or a polymorphonuclear meningitis (12) other forms of onset may resemble an attack of tonsillitis or

may be characterized by vertigo by subungual hemorrhages or by painful fingers or toes due to Osler lesions

The further course of the disease is variable and depends essentially on how soon serious visceral complications occur In milder cases the patient may be active for a long time and attend to his duties without realizing that he is sick

In the absence of serious complications the patient usually runs a long febrile course lasting four to twenty four months or longer during which time he suffers from progressive weakness anemia or cardiac insufficiency Eventually death results from a cerebral accident uremia cardiac failure or an intercurrent infection The duration may be much shortened by an embolic lesion with resulting cerebral or subarachnoid hemorrhage coronary occlusion or rupture of a large vessel or organ Usually there are evidences of repeated embolization numerous organs being involved before the final fatal complication occurs During this period the patient may have intervals of apyrexia and of tolerable comfort Sometimes one is amazed at the optimism that these patients express in speech and behavior despite the fact that they have a relatively short time to live *spes endocarditica* of Horder

Symptoms and Signs

Once the disease is established the most frequent symptoms and signs are the following chills fever sweating anemia emaciation cardiac symptoms renal phenomena splenic enlargement petechiae tender cutaneous lesions purpura pulmonary symptoms tender sternum change in the color of the face gastrointestinal symptoms joint pains joint swellings ocular changes and peculiar pains in various parts of the body

Before discussing the symptoms and signs referable to individual organs we may group the various features of the disease under three headings (1) general symptoms (2) vascular symptoms due to embolism or to local inflammation (3) cardiac symptoms and signs

Certain symptoms are not readily classified under these headings because it is uncertain whether they are due entirely or in part to toxic effects on the blood vessels or to embolization These include petechiae purpura tender cutaneous lesions and possibly the partial glomerular lesions the so called focal embolic glomerulonephritis

(1) *General Symptoms* — The general symptoms result from the toxemia of the infection Fever is the constant feature The course of the fever is variable It may be irregularly remittent or intermittent The fever curve may resemble that of malaria It is apt to be low at first

and higher later If one has the opportunity to observe cases for a long period one not infrequently finds that the fever will be moderately elevated for a period of perhaps a week or two then will regress for some days to a lower level and then swing up to a higher temperature than at any time previously After two or more such waves the temperature curve follows no special course Periods of apyrexia or subfebrile temperature may be observed for a week or two at a time especially if uremia develops The fever may subside temporarily during the administration of drugs such as the sulfonamides

Chills are an inconstant feature but they are apt to occur at some stage of the disease Sometimes chills occur twice daily They may follow intravenous therapy Occasionally a patient runs a severe course with sharp daily swings of temperature up to 105° F and repeated chills Profuse sweats usually occur in such cases but sweating of a moderate degree is common in most of the patients with fever Early sweating is not usually so prominent a feature of this disease as it is of rheumatic fever Night sweats when repeated may suggest pulmonary tuberculosis

Progressive anemia which may reach a severe grade is a common occurrence in subacute bacterial endocarditis It may be the most striking manifestation of the disease and the one which brings the patient under medical care Certain other general symptoms probably are due in part to the anemia These include weakness breathlessness and excessive fatigability

Weakness usually is an early and prominent symptom The patient may note merely that he is more tired than usual at the end of the day or after ordinary activities More often especially as the disease continues the patient complains specifically of weakness or exhaustion On the other hand there are patients who have a sense of relative well being for a long time or who feel well except when the temperature becomes moderately or greatly elevated Weakness when present may be due not only to anemia but also to fever toxemia and loss of weight

Loss of weight may be an early symptom and one of the chief complaints when the patient first consults his physician During the course of the disease the patient usually suffers more and more from anorexia as a result of the fever and toxemia Furthermore nausea and vomiting may develop also Consequently the patient s food intake diminishes progressively and he loses flesh and strength Enormous weight losses are observed occasionally After several months the patient may appear emaciated even though as is usual he was well nourished at the beginning of the disease

Diffuse pains are common especially in cases of long duration While

some of these undoubtedly are due to emboli in various parts of the body others are of a more general nature and may be attributed to weakness toxemia anemia or periostitis Tenderness of the sternum not infrequently is present Insomnia may be an annoying symptom

(2) *Vascular Symptoms* — Vascular symptoms represent more characteristic evidence of subacute bacterial endocarditis and are valuable for diagnosis The great variety of vessels and corresponding organs which may be affected accounts for the multiple symptoms and the varied clinical pictures which are encountered in subacute bacterial endocarditis The emboli as a rule affect arteries of large and medium size but smaller arteries such as the central artery of the retina may be blocked also Arterioles and capillaries often are occluded thereby giving rise to some of the most characteristic symptoms of this disease The small vessels in the kidney and skin undergo changes the nature of which is uncertain insofar as they may be due either to embolic lesions or to local inflammatory changes

Weakness or paralysis of an extremity may result from occlusion of a major artery such as the popliteal the femoral the iliac the radial or the brachial A riding embolus at the bifurcation of the abdominal aorta may cause abdominal or lower back pain weakness coldness and loss of pulses in one or both of the lower extremities Hemiplegia paralysis of facial and ocular muscles aphasia visual and a variety of other disturbances may be produced by cerebral vascular closures A mycotic aneurysm may cause general or local symptoms in the nervous system by pressure or by way of hemorrhage due to rupture Subarachnoid or intraventricular hemorrhage may result

The vessels of the heart lungs and abdominal viscera may all suffer from embolic occlusion Cough hemoptysis fever and to a lesser extent dyspnea and cyanosis may result from closure of branches of the pulmonary artery with consequent infarction of the lung Embolism of the left coronary artery may cause sudden death or greatly shorten the course of the disease Embolism of the right coronary artery which need not of itself be fatal may be suspected from the sudden occurrence of precordial pain and a great enlargement of the liver especially if associated with sino auricular block It is of interest to note that a number of years ago Kinsella in his experimental work observed in one dog an embolism of the right coronary artery accompanied by sinoauricular block Embolism of the larger renal arterial branches may cause pain in the lumbar region the abdomen or in the iliac region hematuria and other urinary symptoms Embolism of the splenic artery or its branches may lead to asymptomatic infarcts but frequently there results extreme pain in the region

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icterus is merely an evidence of the general infection and is seen not uncommonly in bacteremias with pyogenic organisms whether or not endocarditis is present

While a host of skin lesions have been described in cases of subacute bacterial endocarditis there are four types which are encountered with great regularity and are most characteristic and valuable for diagnosis These are (1) petechiæ (2) Osler lesions (3) Janeway lesions and (4) subungual splinter hemorrhages

Petechiæ — Petechiæ with or without pale whitish or yellowish centers are the commonest skin lesions in the disease being observed in at least 80 per cent of the cases Those with the pale centers are more significant The whitish point or streak may be situated off the center of the petechia or may merely indent the circumference Unlike the petechiæ seen in cases of staphylococcemia the white centers are not elevated The petechiæ are found most frequently and best sought for in the conjunctivæ especially of the lids in the fundus in the skin above the clavicles and in the oral mucosa particularly that of the hard and soft palate and near the labial commissures

Discovery of the petechiæ in the conjunctivæ is not always accomplished by casual examination It is often necessary to evert the lids carefully and then meticulously to inspect every part of the conjunctiva with a strong light Pressure on the lid makes the conjunctiva pale so that the petechiæ stand out by contrast One must distinguish small prominent conjunctival capillaries from petechiæ On the surface of the body tiny hemangiomata sometimes are mistaken for petechiæ In the oral mucosa the petechiæ of the disease may be simulated by traumatic hemorrhages

The petechiæ may be isolated but more often they occur in crops which disappear after several days and recur from time to time If the venous and capillary pressure in the forearm is elevated by compression of the arm with the blood pressure cuff petechiæ may appear readily Rumpel Leede phenomenon indicating excessive permeability or fragility of the small vessels The petechiæ may be part of a generalized purpura This in turn may be associated with thrombocytopenia or with a normal number of blood platelets Usually the petechiæ are considered to be due to embolization although bacteria are not found in the lesions French pathologists believe that local inflammatory vascular lesions are responsible for petechiæ In general the petechiæ may be due to embolization and changes in the blood or in the walls of blood vessels

The petechiæ even those with white centers are not pathognomonic of subacute bacterial endocarditis Not only do they occur in the acute

of the spleen The superior mesenteric artery or its branches and rarely the celiac artery may be blocked also by an embolus Such occlusion results in infarction or gangrene of portions of the intestine with consequent severe abdominal pain vomiting, melena or hematemesis

Vascular lesions of the arterioles and particularly of the glomerular capillaries of the kidney whether embolic or inflammatory are extremely common and usually cause albuminuria and microscopic or more rarely macroscopic hematuria In occasional cases in which these lesions are extensive, they may cause azotemia and even well defined symptoms of uremia In the skin similar embolic or inflammatory lesions of the arterioles and capillaries account for at least some of the petechiæ Osler lesions and the Janeway lesions These will be considered in greater detail in the discussion of cutaneous manifestations Similar lesions of the small vessels produce conjunctival petechiæ as well as hemorrhages exudates and degenerative and inflammatory changes in the retina

(3) *Local Cardiac Signs* — The local cardiac signs are due to the underlying valvular or congenital cardiac deformity and to the bacterial endocardial vegetations There may be evidence of cardiac enlargement and various types of murmurs due to a previous rheumatic valvular deformity to a congenital lesion to deformation or perforation of the cusps by the bacterial vegetations or merely to fever and anemia Changes in the character of the murmur or the appearance of new murmurs may occur during the course of the disease The cardiac and circulatory evidences of subacute bacterial endocarditis will be discussed in greater detail on subsequent pages

Symptoms Referable to Individual Organs

The Skin and Mucous Membranes

Pallor of the skin and mucous membranes is an almost constant feature which becomes more and more obvious as the disease progresses One of us has applied the term café au lait to a type of pallor which characterizes the appearance of many patients with subacute bacterial endocarditis Not infrequently there is a pasty pallor like that seen in patients with renal insufficiency and severe secondary anemia Often the patients have a weary look expressive of their sense of fatigue or weakness Rarely there is an erythema of the nose and adjacent parts of the cheeks slightly resembling in appearance the lesion of acute lupus erythematosus We have observed also rare instances of jaundice in cases of subacute bacterial endocarditis due to the gonococcus The

as well as the subacute form of the disease but they are seen also in other conditions such as Libman Sacks disease leukemia and other hemorrhagic diseases including scurvy renal insufficiency carcinomatosis with metastases to the bones and various forms of general bacterial infections

Osler Lesions (*Osler Nodes*) — These tender cutaneous lesions are less common but more specific than petechiæ They are observed in at least 50 per cent of the cases These lesions were described first by Heubner in 1899 and reported in some detail by Rapin in 1903 on the basis of cases seen thirty years earlier Revilliod reported them in 1901 and deserves credit for recognizing their diagnostic importance But it was Osler who made the profession aware of the frequency and diagnostic value of these lesions after finding them in 7 out of 10 cases described in 1909 F Parkes Weber gave the name Osler s sign to them in 1912

The Osler lesions are small usually raised red lesions about the size of a pea but sometimes larger and often smaller They may have a whitish center which gives the lesion an urticarial appearance or they may have a violaceous hue They occur most frequently on the fingertips under the nails on the pads of the toes the soles of the feet in the thenar or hypothenar eminences less commonly on the sides of the fingers the forearms the ear and rarely on the trunk They are observed on the upper extremities more often than on the lower

The essential distinguishing feature of these lesions is that they are always tender Often also they may give spontaneous pain in fact painful fingers may be the earliest or the chief complaint of the patient The French refer to this type of case as the acroalgesic form of the disease In a recent case the eruption of slightly papular lesions about 3-4 mm in diameter resembling Osler lesions were accompanied by violent pain The patient became weak had profuse perspiration the pulse was thready and the systolic blood pressure was 90 Three or four lesions appeared at one time There were three such episodes three days apart It was necessary to administer morphine on each occasion The lesions were noted on the ulnar surface of both hands and wrists and on one occasion also on one leg and forearm The lesions near the nail may be mistaken for panaris (false whitlow) The patient sometimes can predict the appearance of Osler lesions because of antecedent peculiar local sensations or pain The Osler lesions are fleeting and may disappear after a number of hours (nodosités cutanees éphémères) Usually they last four to five days but tenderness may be present only the first two days An Osler lesion may appear on the palm accompanied by a large area of swelling lasting a week or more Sometimes the Osler lesion

is discovered only when systematic palpation of the tip of each finger and toe and the webs of the toes elicits sharp tenderness

As a rule the Osler lesions are bland and disappear without breaking down but rarely necrosis or suppuration occurs In one case of streptococcus viridans endocarditis in which an Osler lesion became purulent we found the pus to contain *Staphylococcus albus* In another patient who had suffered a hemiplegia Osler lesions on the forearm of the paralyzed side became necrotic while those on the normal side did not This observation is of interest in connection with other variations in clinical phenomena on the paralyzed side of hemiplegics

Until recently the Osler lesions were regarded as embolic although Revilliod suggested that they were caused by local vascular changes Recent histological studies by French workers particularly by Merklen and Wolf indicate that these cutaneous nodes are probably due to local possibly toxic or allergic inflammatory changes in the walls of the superficial cutaneous arterioles and capillaries According to these studies the Osler lesion results from vascular occlusion not by emboli but by arteriolitis and especially by an endotheliolitis The center of the node is occupied by a necrotic mass The neighboring capillaries or arterioles on the deep surface of the Malpighian layer of the skin show intense endothelial proliferation and desquamation with partial or complete occlusion of the lumen by the intimal thickening or by secondary thrombosis There is a perivascular inflammation of polymorphonuclear leucocytes and histiocytes and a diffuse cellular infiltration in the dermis and about the sebaceous glands and nerve endings

However it is still uncertain whether emboli may not also play a part in the production of these lesions Thus Osler lesions are seen occasionally in cases in the bacteria free stage of the disease in which there is no fever or toxemia and the vegetations are calcified In such cases the nodes may be presumed to be of embolic origin On one occasion the Osler lesion was observed in a case of Libman Sacks disease Its occurrence in this diseases suggests a local vascular origin With this uncommon exception the Osler lesion has never been seen by us in any disease other than subacute bacterial endocarditis it is therefore considered practically pathognomonic of the latter

Janeway Lesion —Another characteristic skin lesion which one of us has stressed and which was demonstrated to him by his teacher Edward G Janeway was termed the Janeway lesion (Fig 6) In 1897 Janeway wrote that he had several times seen numerous small hemorrhages with slightly nodular character in the palms of the hands and the soles of the feet when possibly the arms and legs had but a scanty crop



FIG 8 Subacute bacterial endocarditis active stage Janeway lesions

Lichenoid eruptions have been described in two cases Soutter observed acuminate papules which resembled lichen scrofulosorum The papules appeared in crops associated with purpuric spots In Weisenbach s case the lichenoid eruption appeared after the patient had been receiving bismuth and arsenic for two months Vesiculobullous eruptions such as described by Davis and Ayman have never been observed by us in patients with subacute bacterial endocarditis In the three cases described by Coombs there were present hemorrhagic bullae but all three patients had been receiving iodides Lesions consisting of bullae and scattered hemorrhagic papules and pustules resembling the hydroa of Bazin have been noted also We have observed a brilliant somewhat elevated erythematous lesion of the palms and soles with scalloped margin and yellowish center somewhat resembling the fixed eruptions due to phenobarbital or antipyrine Milder forms of this eruption are not significant

Erythema multiforme occurs occasionally but we have never seen erythema nodosum in this disease Neither have we seen urticaria a lesion which is not uncommon in active rheumatic fever Erythema annulare a specific lesion of rheumatic fever has not been observed by us in uncomplicated subacute bacterial endocarditis but it has been reported by other observers

Clubbing of Fingers and Toes

Clubbing of the fingers and toes may be considered here because this sign usually is observed in the course of examination of the skin The frequent occurrence of clubbing in subacute bacterial endocarditis was reported by Cotton in 1920 Figures as to its incidence are unreliable and depend on the care with which this phenomenon is specifically sought In a continuous series of 100 cases of subacute bacterial endocarditis which one of us (C K F) examined personally clubbing of the fingers was observed in 68 patients Clubbing of the toes is more difficult to evaluate but it is not infrequent Clubbing of the fingers varies greatly in degree in most instances it is mild compared to the clubbing in cases of bronchiectasis or congenital heart disease True clubbing often can be distinguished from constitutional bulbous fingers by the red margin of skin around the nails in the former Clubbing is most significant for diagnosis if it appears *during the course of the disease while the patient is under* observation It is possible for the clubbing to recede if the patient recovers from the endocarditis or enters the bacteria free stage of the disease

While the Janeway lesion is most characteristic of the acute form, it is also observed in subacute bacterial endocarditis

The term Janeway lesion now has a broader connotation than Janeway s original description gave to it It is applied to small erythematous as well as partially hemorrhagic lesions from 1 to 4 mm in diameter which may be macular or papular in character The macules at least in the beginning blanch on pressure and may leave a fawn colored pigmentation They occur most often on the palms the soles the fingertips or the plantar surface of the toes More rarely these lesions may be scattered diffusely over the extremities and trunk as a maculo papular eruption When the Janeway lesion is present only in isolated form on the palm or sole it is easily overlooked since its margins may blend imperceptibly with the surrounding pink of the skin We have found that discovery of this lesion is greatly facilitated if the arms and legs of the patient are elevated for a few moments so as to blanch them The Janeway lesion after this procedure stands out in sharp contrast to the pale normal skin

Unlike the Osler lesion the Janeway lesion is never painful nor tender Sometimes Janeway lesions and Osler lesions are present simultaneously in the same patient As already noted the Janeway lesion occurs in both acute and subacute bacterial endocarditis especially the former while Osler lesions are found only in cases of the subacute disease In cases of subacute bacterial endocarditis the Janeway lesion is more apt to appear as a flat erythematous macule without the hemorrhagic purplish center seen in the acute cases The variants of the Janeway lesion possible differences in its appearance in the acute and subacute cases, its histology and pathogenesis require further study

Splinter Hemorrhages —Subungual hemorrhages were described by Blumer and by Horder in cases of subacute bacterial endocarditis Because these hemorrhages appear often as characteristic linear streaks resembling a splinter under the nail they have been called splinter hemorrhages Often there is tenderness on pressure over the affected nail bed but this may be due also to an Osler lesion

Other Cutaneous Lesions —A variety of other cutaneous lesions have been described in isolated cases of subacute bacterial endocarditis Their infrequency raises doubt that they are essential features of the disease Analysis of some of the case reports leads one to believe that instances of rheumatic fever or of bacteremia without endocarditis have been mistaken for cases of subacute bacterial endocarditis Finally it is important to exclude toxic eruptions due to medication which the patient has been receiving this is especially true in this period when sulfonamides are being used

in only one case We have observed other isolated instances of this combination since this study was made It is unusual for subacute bacterial endocarditis to develop in a patient in whom auricular flutter or fibrillation is already established These observations are of diagnostic value in that the presence of auricular fibrillation makes the diagnosis of subacute bacterial endocarditis unlikely unless there are definite unequivocal evidences of the disease Auricular fibrillation may appear with embolization of the spleen or kidney in the absence of pain This has been observed by us in hypo ensitive individuals Auricular flutter paroxysmal tachycardia gallop rhythm and premature contractions have been noted

The most frequent disturbance in cases of subacute bacterial endocarditis is a prolongation of the auriculoventricular conduction time P–R interval 0 21 to 0 36 second which is observed in about 15 per cent of cases There are no available studies from which to determine whether these conduction disturbances are due to a concomitant active rheumatic infection Rarely there is a widening and notching of the Q R S complex Bundle branch block has been noted the disturbance having been due in one case to the pressure of a bacterial aneurysm of the sinus of Valsalva on the interventricular septum Complete heart block also has been reported The Stokes-Adams syndrome has resulted from bacterial vegetations on the interventricular septum in the region of a congenital defect

Pericarditis — A pericardial rub is heard infrequently in cases of subacute bacterial endocarditis The possible causes of pericarditis have been mentioned above under Pathology

Cardiac Failure — Cardiac failure is not a prominent feature during a large part of the active disease However some degree of cardiac failure is frequent although its symptoms except in the cases mentioned are submerged by the general toxic and embolic manifestations This point has been emphasized because many physicians have believed that subacute bacterial endocarditis could not be present without evidence of heart failure Furthermore in the early stages of the disease when the diagnosis is most difficult one must not expect evidences of cardiac failure since usually it is the well-compensated and efficient cardiac patient who is affected by subacute bacterial endocarditis When cardiac failure is present early it remains to determine to what extent an active concomitant rheumatic infection is responsible although the studies of Buchbinder and Saphir fail to show a close correlation The great frequency of chronic passive congestion of the viscera when examined at autopsy corresponds to the frequency of cardiac failure toward the end of the disease

A complete list of symptoms which may result from cardiac failure

The Heart and Circulation

Murmurs — From the point of view of diagnosis the important cardiac manifestations are those indicating the existence of previous organic disease Diastolic murmurs particularly the basal diastolic murmur of aortic insufficiency or the apical presystolic murmur of mitral stenosis are the most significant Systolic murmurs frequently are present but must be interpreted with caution as indicating the presence of endocarditis or organic valvular disease Systolic murmurs are heard frequently in the presence of many febrile diseases especially those associated with a general infection whether or not there is an associated endocarditis The same observation is frequent also in patients with anemia which it must be remembered is common with subacute bacterial endocarditis However if the systolic murmur is extremely loud or coarse and especially if it is associated with a thrill or definite preferably roentgenologic evidence of cardiac enlargement it may be assumed that there is congenital or acquired valvular heart disease

In addition to the evidence of previous cardiac or valvular deformities there are often cardiac signs produced by the bacterial endocardial infection itself Thus murmurs may be produced by vegetations which can cause functional valvular stenosis or may be caused by a valvular insufficiency due to ulceration of the valve flap or cusp by the vegetation or be due to the perforation of a cusp by an aneurysm or result from the rupture of chordae tendineae or very rarely from perforation of the interventricular septum Under any of these circumstances a murmur previously present may become more intense or its quality be modified and its site of greatest intensity or its radiation be altered New murmurs may be added to those already present or they may develop when none were there previously Not infrequently an aortic diastolic murmur appears as a result of bacterial endocarditis of the aortic valve independently of a previous aortic insufficiency An interesting feature is the appearance of a very sharp first sound in the presence of a systolic murmur without mitral stenosis A presystolic murmur and a thrill may develop as a result of functional stenosis of the mitral valve due either to a large vegetation a ball valve thrombus or an aneurysm of the anterior mitral flap It is remarkable that in many cases the signs of a valvular defect change very little over long periods of time

Arrhythmia Disturbance of Conduction — Arrhythmias and disturbances of conduction are rare in comparison with their frequency in active rheumatic fever In a series of 109 cases of active bacterial endocarditis Rothschild Sacks and Libman observed auricular fibrillation

Pain in the left upper quadrant of the abdomen and vomiting are common symptoms resulting from infarction of the spleen. This complication may be the first clinical manifestation of the disease. The pain may radiate to the precordium and shoulder and there may be tenderness of the left trapezius muscle if the infarction touches the diaphragm. There may be local tenderness and muscular rigidity over the splenic region. Occasionally a palpable or audible friction rub over the spleen may lead to a diagnosis of dry pleurisy which is uncommon in this disease.

Many infarcts of small size may occur without significant symptoms. On the other hand the splenic infarct may be huge and cause serious complications. Extensive infarction or softening of the infarcts usually is associated with high fever and leucocytosis. Rarely infarction of the spleen is followed by rupture of the organ and intraperitoneal hemorrhage with or without the previous development of a subcapsular hematoma. If the infarct is infected rupture may result in a subdiaphragmatic abscess or peritonitis.

Genitourinary Tract

Hematuria is an important diagnostic feature of subacute bacterial endocarditis. Frank grossly visible hematuria is due usually to large infarction of the kidney. As a rule there is only a microscopic hematuria. Albuminuria is almost invariably present accompanied by various types of casts. The amount of albumin in the urine depends in part on the presence and extent of the glomerular lesions and infarcts.

Infarction of the kidney causes not only hematuria but also pain which may be quite intense. The pain may be situated in the lumbar region or loin or it may radiate to the abdomen the inguinal region or the genitalia. The ureteral radiation of pain may be due to the passage of blood clots down the ureter. Occasionally there is pain just above the crest of the ilium. This is apt to occur when there is infarction of the posterior part of the kidney. The presumption is that the resulting inflammation of the capsule implicates the roots of the iliohypogastric nerve. The pain often is associated with local tenderness and muscle spasm as well as with vomiting. This combination of symptoms sometimes leads to an erroneous diagnosis of a *surgical abdominal complication* and consequent laparotomy. When the kidney is enlarged and palpable the exact site of infarction can be determined at times by eliciting localized tenderness by means of systematic palpation of the front and back of the kidney with one hand in the lumbar region and one on the abdominal wall.

is not relevant to this discussion. We have no accurate data as to the relative frequency of right sided and left sided heart failure in subacute bacterial endocarditis. Dyspnea on exertion and less often, orthopnea and paroxysmal nocturnal dyspnea are fairly common complaints. It is uncertain how often the dyspnea results from pulmonary congestion secondary to left sided heart failure and how often it is due to anemia, pulmonary complications, general weakness or other consequences of the toxemia. That anemia may play an important role is seen in the disappearance or improvement of dyspnea when the patient's hemoglobin is elevated by a transfusion. The evidences of left and right ventricular failure are the same as under other conditions. Abdominal distress or pain and a variety of gastrointestinal disturbances may be caused by right ventricular failure, but they may be due also to visceral emboli.

Precordial Pain. — Precordial pain, occasionally of great intensity and with the typical radiation of angina pectoris, may be present. Usually it occurs in patients with aortic valvular disease and may have no connection with the bacterial endocarditis as such. We have observed also irradiated precordial pain as a result of splenic infarction. We have several times observed patients who were found at autopsy to have emboli in their coronary arteries without having presented any clinical picture of coronary occlusion.

Ball valve Thrombus in Left Auricle. — Occasionally a characteristic clinical picture results from a ball valve thrombus in the left auricle which occludes the mitral orifice. There are evidences of shock including low blood pressure and cold extremities, bluish mottling of the extremities followed by cyanosis, necrosis or patchy gangrene of the tips of the fingers, toes and nose, as well as pulmonary edema. The ball valve thrombus may occlude the mitral valve intermittently, the symptoms subsiding between attacks. This syndrome occurs more often preterminally. With the occurrence of a ball valve thrombus a systolic murmur previously present may disappear and the first sound diminish in intensity.

Spleen

The spleen is enlarged almost invariably. It is clinically palpable in about 80 to 90 per cent of the cases. Although large, the spleen may be not palpable clinically either because the enlargement is of only moderate degree or because the spleen is fixed to the diaphragm by adhesions. Occasionally, when the spleen is huge, extending to the level of the umbilicus, an erroneous diagnosis of leukemia, Banti's disease or some other splenic disease is made.

farcts caused by prolonged pulmonary congestion or to pulmonary apoplexy

Pulmonary emboli occur uncommonly because the bacterial vegetations are predominantly on the left side of the heart However when the endocardial vegetations are on the right side of the heart as in cases of congenital heart disease or when there is a patent foramen ovale or a patent ductus arteriosus pulmonary emboli may occur In such instances there are cough hemoptysis and a variety of pulmonary signs which dominate the clinical picture

Chest pain may be due to lobar pneumonia or pulmonary infarction Dry pleurisy is rare Occasionally there is a clear or hemorrhagic pleural effusion which may occur independently or be secondary to a lobar pneumonia or to a pulmonary or splenic infarct Pulmonary edema may be the result of a lobar pneumonia or of left ventricular failure Hydrothorax is common toward the end of the disease it is probably a manifestation of cardiac failure

In several cases we have observed hoarseness as a symptom of the disease It may be temporary or permanent In all of the cases with hoarseness which were due to paralysis of the left recurrent laryngeal nerve the patient had a patent ductus arteriosus In one patient hoarseness persisted even though the patient recovered spontaneously from a complicating subacute bacterial endocarditis The hoarseness in these cases probably is due to the pressure of an enlarged pulmonary artery on the recurrent laryngeal nerve The enlarged pulmonary artery found in cases of patent ductus arteriosus may become further dilated as a result of cardiac failure developing in the course of bacterial endocarditis

Gastrointestinal Tract and Liver

Disturbances of the gastrointestinal tract are common They sometimes occur early and may be conspicuous Anorexia postprandial distress and abdominal pain are the commonest symptoms referable to this site Nausea and vomiting usually are late symptoms which may be associated with cardiac insufficiency uremia or a cerebral complication or may be due to intense toxemia or visceral embolization Abdominal distress may be due to congestion of the liver and intestinal tract as a result of cardiac failure Abdominal pain sometimes of great intensity usually is due to infarction of the spleen kidney or intestinal tract but the explanation is not always at hand Diarrhea is uncommon except when due to independent causes or to uremia It may occur with or without achylia Occasionally there is gross or occult blood in the stool

Renal insufficiency occurs more frequently than is generally recognized We have observed it in some degree in one third of a series of 100 active cases (C K F) More detailed studies of renal function are necessary than are at present available Usually renal insufficiency is denoted by a slight or moderate azotemia urea nitrogen 25 to 75 mgm per 100 c c and a fixation of the specific gravity at 1 010 by the concentration test Azotemia of moderate degree may be caused by right ventricular failure independent of true renal insufficiency The latter when present may be due to very numerous partial glomerular lesions or oftener to diffuse glomerulonephritis However uremia develops much less frequently than in the cases in the bacteria free stage In the presence of renal insufficiency failure of the heart may contribute to the onset of uremia The symptoms of uremia are similar to those ordinarily encountered in that condition Despite the presence of renal insufficiency the blood pressure almost invariably remains low

Vesical symptoms are not uncommon Frequency of urination urgency of urination pain on urination pain in the hypogastrium and retention of urine are observed When these symptoms are prominent they may erroneously suggest independent disease of the bladder the fundamental endocarditis being overlooked

Amenorrhea is common during the disease Menorrhagia or metrorrhagia may occur as part of a hemorrhagic tendency

Respiratory Tract

Cough is a frequent symptom which may occur early and be quite distressing It is often spasmodic becoming severe late in the afternoon and at night The pathogenesis of the early cough without evidence of any pulmonary disturbance is uncertain Libman has suggested that it results from the pressure on the trachea of enlarged inferior intertracheobronchial lymph nodes (of Poirier) into which the lymphatics of the heart drain These nodes sometimes are very large Cough may be due also to a bronchitis which occurs frequently Late in the disease bronchopneumonia is a common cause of cough It is to be noted that bronchopneumonia even extensive may occur early Aside from other pulmonary complications such as lobar pneumonia or pulmonary infarction cough has been attributed to pulmonary congestion associated with left sided heart failure and to minute emboli in the bronchial arteries

While the cough may be dry in its early stages usually it is associated with mucopurulent or hemorrhagic expectoration Hemorrhagic sputum may result from pulmonary infarction lobar pneumonia stasis in

dizziness and vomiting, they include stiff neck, exaggerated or absent deep reflexes, and positive Kernig and Brudzinski signs. The spinal fluid varies considerably. Occasionally it is normal despite meningeal signs. There may be a serous meningitis with the spinal fluid containing an increased quantity of protein and few or many cells, mostly lymphocytes, or the fluid may contain few or many polymorphonuclear leucocytes with or without bacteria. Not infrequently the fluid is bloody or xanthochromic due to a subarachnoid hemorrhage which may occur even in the absence of any local cause (hemorrhagic tendency). Both this and intraventricular hemorrhage give the usual symptoms. Occasionally such subarachnoidal hemorrhage may be ushered in by severe pain to the outer side of the eye. In our experience the intraventricular hemorrhage is fatal always. The patient may recover from the effect of a subarachnoid hemorrhage.

The clinical picture may simulate that of encephalitis. In such cases there may be mental lethargy, somnolence, blurred vision, vertigo, diplopia, salivation, ocular paralyses, mask-like facies, tremor, muscular twitchings or rigidity. In one case which occurred during an epidemic of encephalitis the patient seemed to be suffering from both diseases; a necropsy was not obtained.

Eyes

The occurrence and significance of petechiae in the conjunctiva has been mentioned already. The frequency and diagnostic importance of retinal lesions were stressed first by Litten. Retinal hemorrhages are observed often. These may be flame shaped or circular. The hemorrhages may have a white center. According to Litten these white centered hemorrhages appear identical with those seen in severe anemia and in leukemias. He believed, however, that while the white centers in leukemia are due to an accumulation of leucocytes, those in subacute bacterial endocarditis represented necrosis secondary to embolization. This is uncertain. Doherty and Trubek described the characteristic lesions as "boat shaped" petechiae (Fig. 9). Usually there are recurrent crops of petechiae. The hemorrhages may develop in the course of a few hours. They have been observed with the aid of the ophthalmoscope during their development.

Sometimes there are round white spots in the retina which were described by Roth as being due to "varicose hypertrophy" of the retina. He did not believe that they were embolic in origin. Neither did he recognize their relationship to endocarditis, having observed them in a variety

The liver may be enlarged as a result of chronic passive congestion and may be tender Occasionally this tenderness is associated with rigidity of the overlying abdominal wall and with vomiting a combination which suggests acute cholecystitis or another acute abdominal condition Jaundice which is not very uncommon with acute bacterial endocarditis occurs rarely with the subacute form In two instances of subacute bacterial endocarditis in which we recall the presence of jaundice the causative organism was a gonococcus In one of these cases there was thrombocytopenic purpura severe anemia and a large splenic infarct

Central Nervous System

Lesions of the central nervous system are common in cases of subacute bacterial endocarditis Usually there are arterial lesions including arteritis, with or without thrombosis bacterial emboli and mycotic aneurysms Intracerebral intraventricular or subarachnoid hemorrhage may result from rupture of a mycotic aneurysm or hemorrhagic tendency, while encephalomalacia is produced by vascular embolism or thrombosis Local closure of an artery may occur as a result of arteritis and intimal proliferation with or without thrombosis Small and occasionally large abscesses may be found probably due to autolysis and secondary polymorphonuclear invasion of the infarcted areas

Commonly there is a localized or diffuse meningo encephalitis due to scattered inflammatory and ischemic foci This may involve the cerebrum the cerebellum the cerebral ganglia and rarely the spinal cord A funicular myelosis of the cord has been described once

The symptoms corresponding to all these lesions are so numerous that it would be hardly possible to describe them in full In addition there are cerebral symptoms due to toxemia Headache is common throughout the disease Vertigo especially on rising in the morning or on exertion has been noted occasionally as an early symptom In one instance somnolence which was a prominent symptom was traced by the observer to a lesion in the substantia nigra Toward the end of the disease there may be delirium stupor or coma

When embolic aneurysms rupture they produce pain hemorrhage or symptoms of compression of nearby structures Hemiplegia diplegia with or without aphasia are common symptoms of cerebral embolism The hemiplegia usually occurs suddenly but may be intermittent for two or three days Sometimes the hemiplegia regresses

Signs of meningeal irritation are frequent In addition to headache

cases in which we recently studied sections of the eye with Dr Robert K Lambert the following lesions were observed There were deep hemorrhages in the superficial layer of the retina and deep hemorrhages just below the nuclear layer There were accumulations of mononuclear cells in the retina which did not seem to be lymphocytes but resembled histiocytes The most marked alterations were in the choroid which was tremendously thickened and contained many obliterated arterioles without evidences of embolism or thrombosis There was an intense perivascular cellular infiltration and edema Most of the cells were of the mononuclear variety and included histiocytes and probably young fibroblasts In addition there was a papillitis which was characterized by cellular infiltration and edema

In a variable number of cases there is an optic neuritis This was stressed as a diagnostic sign of subacute bacterial endocarditis by Falconer who found it in 5 out of 15 cases a much higher incidence than we have encountered As noted above the optic neuritis is a true papillitis Occasionally there is choking of the disc and optic atrophy may develop

Visual disturbances including amblyopia and central scotoma may occur as a result of cerebral lesions Sudden blindness occasionally results from embolism of the central artery of the retina Occasionally pain over the eye occurs due to anemia The occurrence of such anemic neuralgia was proven in one case by the disappearance of the neuralgia after the hemoglobin rose as a result of transfusion and its reappearance when the hemoglobin again dropped As already noted above severe pain may occur over the eye at the onset of a subarachnoid hemorrhage Iridocyclitis and panophthalmitis which are not uncommon in acute bacterial endocarditis have never been seen by us in subacute bacterial endocarditis

Joints and Bones

Joint pains are common appearing usually as transitory arthralgias Occasionally there is a true arthritis with swelling of the joints but without superficial redness It is uncertain how often the joint pains may be due to a concomitant active rheumatic fever

Bony pains and tenderness are not uncommon and may form important symptoms of the disease We have found tenderness of the lower half of the sternum to be of particular frequency and a valuable diagnostic sign especially if the hemoglobin is not low Usually it occurs late in the disease and is especially common in the bacteria free stage For

of pyogenic infections with bacteremia They are in fact more often observed in cases of acute than of subacute bacterial endocarditis Because their relationship to endocarditis was recognized by Litten the French termed these lesions Litten's sign But it was Litten who gave

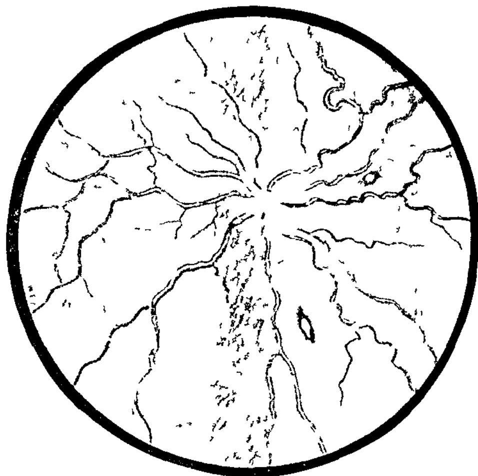


FIG 9 Subacute bacterial endocarditis active stage ocular fundus with papillitis typical boat shaped lesions

them their present name Roth spots In many discussions of retinal lesions these spots are described erroneously as hemorrhages with white centers

Dellmann found that pathologically the Roth spots represented perivascular accumulations of lymphocytes in the nerve fiber layer of the retina which might or might not be surrounded by edema and hemorrhage He considered the lesions secondary to bacterial embolization In two

be less than 20 per cent The red blood count usually is between 3 and 4 million While the color index usually is low not rarely it is almost or equal to 1 It is not above 1 except in the presence of uremia from renal lesions such as occur sometimes especially in the bacteria free stage of the disease

The *white blood count* is quite variable In uncomplicated cases the blood count often is normal or there is a slight leucocytosis In our experience the highest counts over 25 000 were encountered in cases with extensive visceral infarction We have observed a leucocyte count as high as 48 000 in a case with extensive splenic infarction and thrombophlebitis of the splenic vein Moderately high counts may be due to a concomitant lobar pneumonia Leukopenia is not uncommon We have seen a white count of 2 400 in a patient with subacute bacterial endocarditis complicated by lobar pneumonia

The *differential count* also is variable When there is a leucocytosis the polymorphonuclear cells form between 65 and 90 per cent of the leucocytes In such cases there is usually a shift to the left in the Schilling hemogram and the polymorphonuclear cells may show toxic granules In the cases with leukopenia there may be a moderate lymphocytosis Agranulocytosis has been reported in the absence of any special medication but this has not been observed by us

Sometimes the blood contains large phagocytic cells varying in size between 10 and 80 micra These macrophages histiocytes or endothelial cells as they have been variously termed may dominate the blood picture (Van Nuys) and are helpful in confirming the diagnosis But they are not usually present nor are they pathognomonic of this disease When present they usually form 3 to 5 per cent of the leucocytes but may go as high as 40 per cent

The blood platelets usually are normal but severe thrombocytopenia occasionally occurs Diffuse purpura and other evidences of bleeding tendency may be present whether or not there is a reduction in the number of blood platelets Epistaxis has been reported in 3 to 4 per cent of the cases This may be due to a hemorrhagic tendency or to an associated active rheumatic fever

The sedimentation rate usually is rapid in the active stage of the disease

There is a relative and absolute increase in the blood globulin Kurten has used this as the basis of a diagnostic test (formol gel reaction) However this reaction is not a valuable test as it may be negative in the presence of subacute bacterial endocarditis and positive in other conditions such as amyloid disease multiple myeloma syphilis and cirrhosis of the liver

mortem study of the marrow suggests that the tenderness of the sternum is due to regeneration of the bone marrow In making the test the patient should sit up the upper and lower sternum should be tapped for comparison and direct pressure or rubbing should be avoided Although tenderness of the sternum is not pathognomonic of this disease having been found in other conditions including tricuspid valvular defects in an obscure case its presence suggests a consideration of subacute bacterial endocarditis

Severe osseous pains have been noted over the sacrum ischium upper end of the femur and other bones On occasion the pain and tenderness have been severe enough to suggest osteomyelitis The bony pains have been attributed to periostitis to hemorrhages or emboli in the periosteum to pressure of an embolic aneurysm on a bone and to aneurysm of one of the osteal vessels Sometimes there are pain and stiffness of the neck which may develop acutely and may resemble cervical spondylitis The pain may radiate to the shoulder

Occasionally we encounter what might be called a periosteal form of the disease For example in one of our cases the clinical picture was dominated by severe pains in the lower back suspected by the practitioner of being renal in origin right shin and dorsal aspect of the right foot These pains were found to be due to very tender periosteal thickening of the last lower rib the anterior surface of the tibia and the surface of a metatarsal bone Such periosteal lesions have been noted in other bones Care must be exercised lest they be confused with Osler lesions Difficulty may arise in connection with Osler lesions whether they are more superficial and accompanied by marked erythema or deeper with no visible erythema In a recent case in which a periosteal lesion occurred in a metatarsal bone with accompanying redness and swelling of the overlying skin the diagnosis was made definitely by finding that the erythematous swollen skin could be squeezed between the fingers without eliciting pain while the underlying bone was very tender

Blood

A *positive blood culture* of *Streptococcus viridans* or other causative organisms is obtained in the majority of cases This is discussed under etiology and Diagnosis

A *secondary anemia* is characteristic of the disease Usually the hemoglobin averages between 50 and 70 per cent Occasionally a relatively normal hemoglobin is maintained for a long time The hemoglobin is apt to fall progressively during the course of the disease Occasionally it may

be less than 20 per cent The red blood count usually is between 3 and 4 million While the color index usually is low not rarely it is almost or equal to 1 It is not above 1 except in the presence of uremia from renal lesions such as occur sometimes especially in the bacteria free stage of the disease

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Other Symptoms

Several cases of hypophyseal cachexia have been noted (Simmonds Balo) due to embolization of the anterior lobe of the hypophysis Tender swellings of the temporal arteries have been described due to arteritis and also to aneurysm Thrombophlebitis occurs rarely, chiefly in the lower extremities Parotitis has been noted

Diagnosis

The following four features in combination lead to the diagnosis of subacute bacterial endocarditis (1) a valvular defect or a congenital lesion (2) a febrile course (3) embolic phenomena and (4) a positive blood culture

Sterile blood cultures even when repeated do not exclude the diagnosis when the clinical features are definite On the other hand a positive blood culture of a nonhemolytic streptococcus in the absence of significant clinical findings may be of no importance but may merely represent an inconsequential transitory bacteremia As we pointed out many years ago such transitory bacteremias are of frequent occurrence They may take place in the course of a great variety of diseases and even in apparently healthy persons In an extensive investigation of this subject Lichtman and Gross found nonhemolytic streptococci in the blood of about 6 per cent of patients suffering from a great variety of diseases in the wards of the Mount Sinai Hospital In rheumatic fever with active polyarthritis they were found in 8 per cent of the cases studied In chronic cardiovascular disease without active arthritis the figure was 5 per cent In rheumatic fever as a whole the figure was 6 per cent the same as in the general population of the hospital In cases of aplastic anemia and pernicious anemia the blood cultures were positive in 6 per cent Patients who were near the time of death were not included The organisms grown in these cases of *transitory* bacteremia were few in number and as a rule were present only in fluid media When a nonhemolytic streptococcus is obtained on solid media and when active local foci such as mastoiditis or puerperal infection due to nonhemolytic streptococci have been excluded it is likely that one is dealing with a subacute bacterial endocarditis It should be remembered that the blood culture may be only intermittently positive

The presence of definite embolization may be assumed only when there are signs and symptoms of closure of a large vessel in an extremity in the brain kidney spleen mesentery etc In patients with aortic valvular

disease alone embolic vascular closures almost always indicate a bacterial endocarditis active or obsolescent In the presence of mitral stenosis such emboli may come from a thrombus in the left auricle without any evidence of infection The diagnosis of subacute bacterial endocarditis must be made carefully in patients suffering from auricular fibrillation In determining the source of emboli to the above mentioned organs it should be remembered that emboli may arise also from ventricular thrombi or rarely from a vein in a patient with an auricular or ventricular septal defect paradoxical embolus or from a thrombus on an ulceration of a large artery such as the aorta or from an eroded atherosclerotic valve

Other findings the embolic nature of which is less certain are important suggestive or confirmatory signs These include white centered petechiae Osler lesions Janeway lesions and microscopic or gross hematuria

Marked anemia particularly when associated with a café-au lait pallor splenic enlargement and clubbed fingers form a triad very frequently present and should suggest the diagnosis Tenderness of the lower half of the sternum not infrequently is demonstrable It is of more significance for the diagnosis when the hemoglobin percentage is high Macrophages in the blood are supportive evidence but are not demonstrable frequently enough to be of much value in diagnosis They should be sought in the first drop of blood obtained by puncture of the ear

In practice the diagnosis usually is made under the following circumstances If a patient known to have a valvular or congenital cardiac defect becomes febrile without obvious cause definite evidence of subacute bacterial endocarditis must be sought One looks for white centered petechia Osler lesions Janeway lesions and splinter hemorrhages The association of valvular heart disease fever and white centered petechiae usually denotes subacute bacterial endocarditis If this tentative diagnosis is correct confirmation usually is found in the presence of a palpable spleen clubbed fingers secondary anemia and microscopic hematuria Tender areas in the spleen or an evident perisplenitis may be very valuable The diagnosis becomes definite if in addition to these findings there is a positive blood culture especially in plates or if a large artery is occluded by an embolus In cases of subacute bacterial endocarditis which *arises on the basis of an open ductus arteriosus* the vegetations may be entirely on the wall of the pulmonary artery and the symptoms apart from the fever and general symptoms may be largely pulmonary in nature

In the absence of a clinically demonstrable valvular defect or con

genital lesion or arteriovenous aneurysm the diagnosis may be more difficult Fever of unknown origin embolization white centered petechiæ splenomegaly and clubbed fingers all are manifestations which should make one think of the diagnosis and look for corroborative signs

Differential Diagnosis

Because of the multiplicity of symptoms which have been noted already subacute bacterial endocarditis may be confused with a vast number of conditions of which only some can be discussed

The fever may lead to difficulty in differentiation from such conditions as rheumatic fever Libman Sacks disease influenza pneumonia typhoid fever malaria tuberculosis and intra abdominal Hodgkin s disease We *have seen each one of these diagnoses erroneously made in cases of sub* acute bacterial endocarditis before characteristic manifestations were observed On the other hand we have seen a diagnosis of subacute bacterial endocarditis made because a patient with valvular heart disease suffered from fever which subsequently was found to be due to other conditions

Symptoms that speak for *rheumatic fever* are pericardial rub erythema marginatum typical migrating polyarthritis and marked disturbances of the conduction system Of course recently developed subcutaneous rheumatic nodules would be most important Symptoms that would speak for the presence of subacute bacterial endocarditis are white centered petechiæ splenomegaly Osler lesions Janeway lesions and clubbed fingers Positive blood cultures of nonhemolytic streptococci occur only occasionally in rheumatic endocarditis (see above) and then are limited to fluid media Confusion may arise when both diseases are present simultaneously

In *Libman Sacks disease* there is often present the typical eruption of acute lupus erythematosus Not infrequently there is a fibrinous pericarditis The patient is almost always a young adult female As with subacute bacterial endocarditis there may be present infrequently white centered petechiæ hematuria and albuminuria with renal insufficiency and thrombocytopenic purpura Splenomegaly is uncommon there is no clubbing of the fingers or toes and repeated blood cultures are sterile except when there is a late secondary invasion of the blood stream The combination of white centered petechiæ and a pericardial rub suggests Libman Sacks disease since the former are rare with rheumatic fever and the latter is unusual with subacute bacterial endocarditis This combination may be encountered also in patients suffering from both subacute

bacterial endocarditis and active rheumatic endocarditis Under such conditions however the blood culture almost surely would reveal a bacteremia

Influenza and *pneumonia* are erroneously diagnosed early in the disease only because these are common causes of fever because fatigue vague pains dyspnea and cough are frequent symptoms and because the possibility of a bacterial endocarditis is overlooked

Typhoid fever and *malaria* may be considered because of prolonged fever and splenomegaly the latter diagnosis is entertained especially when there are repeated chills and sweats These diseases are distinguished by blood culture by the Widal test by culture of the stool and urine and by examination of blood smears for parasites

Intra-abdominal Hodgkin s disease not infrequently has been diagnosed when there is splenomegaly and fever of uncertain origin While some general enlargement of the lymph nodes may be encountered in subacute bacterial endocarditis large nodes such as those encountered in Hodgkin s disease are not found One must look for such nodes especially above the clavicle behind and along the sternomastoid muscle and in the iliac fossae Pruritus and a characteristic ochre color of the face are suggestive of Hodgkin s disease Transitory invasions by nonhemolytic streptococci may occur in this disease

In connection with *periarteritis nodosa* one must distinguish between clinical and pathological periarteritis nodosa When Kussmaul and Maier described the disease they referred to cases in which there were present aneurysms palpable or visible during life or at necropsy These aneurysms are due to necrotizing arteritis Nowadays the term periarteritis nodosa is used largely for a necrotizing arteritis that is only discovered by microscopic examination at the postmortem table without the presence of real aneurysms These we believe should be designated by the term necrotizing arteritis with or without periarteritis If aneurysms be present the pathological designation would be necrotizing arteritis with periarteritis and aneurysm formation We believe that the term periarteritis nodosa should be employed in the clinical sense as first described by Kussmaul and Maier or be dropped It is necessary to point out that necrotizing arteritis may occur in a variety of acute infections including acute bacterial endocarditis rheumatic endocarditis subacute bacterial endocarditis and Libman Sacks disease This concept was put on record by Mallory as far back as 1913

Aneurysm formation arising from infection in the vascular wall is unusual in acute bacterial endocarditis It is much more common in subacute bacterial endocarditis and is of bacterial origin except in the

genital lesion or arteriovenous aneurysm, the diagnosis may be more difficult Fever of unknown origin, embolization white centered petechiæ, splenomegaly and clubbed fingers, all are manifestations which should make one think of the diagnosis and look for corroborative signs

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Because of the multiplicity of symptoms which have been noted already subacute bacterial endocarditis may be confused with a vast number of conditions of which only some can be discussed

The fever may lead to difficulty in differentiation from such conditions as rheumatic fever Libman Sacks disease influenza pneumonia typhoid fever malaria tuberculosis and intra abdominal Hodgkin s disease We have seen each one of these diagnoses erroneously made in cases of sub acute bacterial endocarditis before characteristic manifestations were observed On the other hand we have seen a diagnosis of subacute bac terial endocarditis made because a patient with valvular heart disease suffered from fever which subsequently was found to be due to other con ditions

Symptoms that speak for *rheumatic fever* are pericardial rub erythema marginatum typical migrating polyarthritis and marked disturbances of the conduction system Of course recently developed subcutaneous rheu matic nodules would be most important Symptoms that would speak for the presence of subacute bacterial endocarditis are white centered pe techiæ splenomegaly Osler lesions Janeway lesions and clubbed fingers Positive blood cultures of nonhemolytic streptococci occur only occa sionally in rheumatic endocarditis (see above) and then are limited to fluid media Confusion may arise when both diseases are present simul taneously

In *Libman Sacks disease* there is often present the typical eruption of acute lupus erythematosus Not infrequently there is a fibrinous pericar ditis The patient is almost always a young adult female As with subacute bacterial endocarditis there may be present infrequently white centered petechiæ hematuria and albuminuria with renal insufficiency and thrombocytopenic purpura Splenomegaly is uncommon there is no clubbing of the fingers or toes and repeated blood cultures are sterile except when there is a late secondary invasion of the blood stream The combination of white centered petechiæ and a pericardial rub suggests Libman Sacks disease since the former are rare with rheumatic fever and the latter is unusual with subacute bacterial endocarditis This combina tion may be encountered also in patients suffering from both subacute

Because of albuminuria, hematuria, fixation of urinary specific gravity, azotemia and anemia a diagnosis of subacute or chronic *glomerulonephritis* sometimes is made without recognition of the underlying endocarditis.

Occlusion, aneurysm formation and rupture of cerebral vessels or diffuse meningo-encephalitis may lead to confusion with primary cerebral or meningeal disease. *Encephalitis* is simulated when there are present such symptoms as a mask-like facies, ocular palsy, muscular twitching and somnolence or delirium. A diagnosis of *meningococcus meningitis* may be made in the presence of meningismus, serous meningitis or bacterial meningitis. This diagnosis may seem to be supported when there is a diffuse petechial eruption but the petechiae are apt to be more violaceous than in cases of subacute bacterial endocarditis. Examination of the spinal fluid and search for other evidences of subacute bacterial endocarditis clarify the diagnosis. It is to be noted that meningitis due to a nonhemolytic streptococcus may occur independently of any endocarditis. When there is a hemiplegia and aphasia a diagnosis of *cerebral thrombosis* or *cerebral hemorrhage* may be made, its relation to an endocarditis being unrecognized.

The gastrointestinal symptoms and abdominal pain may lead to a diagnosis of *appendicitis, acute cholecystitis, abdominal malignancy* or *tuberculosis of the mesenteric lymph nodes*.

Weakness, anemia, petechiæ and purpura may simulate *pernicious anemia, hemorrhagic diseases* or *malignancy*. Unlike pernicious anemia the anemia of subacute bacterial endocarditis is of the secondary type, the color index not being more than 1 except in the presence of renal insufficiency. Furthermore, macrocytes and megaloblasts are absent in cases of subacute bacterial endocarditis.

The splenomegaly and anemia of the disease may be mistakenly ascribed to *Banti's disease, thrombosis of the splenic vein, Hodgkin's disease* or some other form of splenic disease. We have on occasion witnessed an erroneous diagnosis of *cirrhosis of the liver* made due to the presence of a large, hard liver and a large spleen. *Hepatic suppuration* and *subphrenic abscess* have been considered in the presence of fever of unknown origin accompanied by pain in the region of the liver, tenderness, elevation of the diaphragm and perihepatitis. Unnecessary operations have been done on a number of occasions.

Because of pains in the bones and tenderness, perhaps due to periosteal lesions, *bone tumors* may be diagnosed. Bony pains and local tenderness may produce a picture resembling *osteomyelitis*.

Acute bacterial endocarditis often can be distinguished by the presence

rare instances of aneurysms due to impact (see later on in discussion of bacteria free stage) In the necrotizing arteritis that occurs in subacute bacterial endocarditis bacteria are not demonstrable (Helpern and Trubek) Such necrotizing arteritis free from bacteria in a case in which the endocardial lesion is definitely bacterial must be regarded as a toxic (allergic) effect of the infectious agent Unfortunately the cause in cases of periarteritis nodosa is unknown Eosinophilia as is well known need not be present in periarteritis nodosa In other words when necrotizing arteritis is encountered always one must try to find the cause and to remember that in some of the cases the origin lies in the various conditions associated with endocarditis

Pulmonary tuberculosis may be diagnosed because of the fever weakness anorexia loss of weight and cough Occasionally this error arises in cases in which the endocardial lesions are confined to the right side of the heart or pulmonary arteries and emboli are limited to the pulmonary circulation *Bronchopneumonia lobar pneumonia* and *other pulmonary diseases* are diagnosed when the major symptoms are respiratory Sometimes these conditions are present as complications of the endocarditis Therefore one must always keep an underlying cause in mind

The diagnosis of *Graves disease* has been made because of fatigability, weakness sweating loss of weight nervous symptoms and high basal metabolic rate The increase in the basal metabolic rate in bacterial endocarditis may be due to the fever alone However it has been claimed by Gessler that the increase in rate is often out of proportion to what can be ascribed to the fever alone but his observations need confirmation In coming to a conclusion in a given case it must be borne in mind that a patient suffering from Graves disease may develop subacute bacterial endocarditis Besides we have noted cases in which the endocardial infection apparently set up hyperthyroidism

Vesical tenesmus frequency of urination pain in the loin and hematuria caused by renal infarction and the passage of blood along the ureter have led to unnecessary operations for suspected *disease of the kidney* such as *renal tuberculosis calculi* or *pyelonephritis* In several instances a kidney has been removed unnecessarily If operation is performed because of a mistaken diagnosis of surgical renal disease it is important that the surgeon recognize the characteristic flea bitten kidney or the infarcts which are usually ochre colored as pointing to bacterial endocarditis as the primal cause and forego nephrectomy Pain in the lumbar region associated with tenderness and muscle spasm may be so severe in infarction of the kidney that an erroneous diagnosis of perinephric abscess may be made

likely to be encountered If anemia is present it may or may not be severe When anemia is present in marked degree it is of assistance in making a diagnosis as are also splenic involvement and the development under observation of clubbing of the fingers It is also important to look sharply for tenderness of the lower sternum white-centered petechiae Osler lesions meningismus which not infrequently is a symptom of the disease in general and for macrophages in the blood obtained from puncture of an ear It is necessary to collect such cases and make a detailed description of the clinical features in order to avoid the difficulties encountered in differentiating them from other conditions which may simulate them such as tuberculosis anemias mild rheumatic fever hyperthyroidism so called neurasthenia etc There is greater difficulty in diagnosis when a valvular defect is not demonstrable

The blood culture practically always is positive at one time or another in these mild cases particularly if special methods are employed As in the more marked forms of the disease one does not always find a streptococcus In one of our cases a Gram negative diplococcus *Neisseria flava* was recovered twice Immunological aid is needed for the clinical recognition of subacute bacterial endocarditis particularly mild cases and those in the bacteria free stage as discussed on a later page

It is difficult to estimate with precision the duration of subacute bacterial infections of the endocardium and especially in the mild cases While the latter appear to be essentially of rather short duration even as short as three weeks they may last for a long time One of the cases which we observed had a duration of six months and another of at least one year The most remarkable mild case was that of a man thirty years of age at the time who gave a history of being ill since September 1922 and came under observation in November 19 3 The duration of his illness had been almost three years the period of observation almost two years Except for the short periods during which he suffered from pulmonary complications the rectal temperature for weeks at a time did not rise above 99.4 F After his recovery in 19.5 he looked well and regained his full weight The spleen was just palpable but had been larger The valvular lesion was an aortic insufficiency White centered petechiae were present on a number of occasions and the sternum for some time was very tender From November 19.3 his blood was cultured fifteen times The cultures that were positive showed non hemolytic streptococci by the ordinary aerobic methods as well as by the modified Smith Noguchi method The final positive blood culture was obtained by means of the last designated method and was negative aerobically The results of blood cultures were as follows

of an active local infection a pyogenic organism in blood cultures a briefer course and by the development of suppurative metastases

In cases of abortion or normal labor subacute bacterial endocarditis may have to be differentiated from a *puerperal infection* The diagnosis of bacterial endocarditis then must be based on the presence of Osler lesions on the development of a definite organic valvular murmur or embolization explainable as coming from the left side of the heart

MILD CASES OF SUBACUTE BACTERIAL ENDOCARDITIS

It has been noted on a previous page that even in the so called active bacterial cases of the usual type there may be short periods during which the patient has little or no fever carries on his usual activities and feels relatively comfortable The existence of mild forms of the disease has been known since the description of a mild febrile disease was given by Oille Graham and Detweiler in 1915 Twenty three cases were described the blood cultures of all of which revealed a nonhemolytic streptococcus All of these patients recovered In 1920 Salus reported 18 similar cases At the present time the classification of these cases cannot be considered determined They served however to draw attention to cases of subacute bacterial endocarditis which were mild throughout their course It must be remembered that early in the ordinary type of case the picture may be mild for many weeks

Capps Biggs Major F Janney Smith and others have described similar cases occurring sporadically These cases need further careful consideration This is important because of the frequency of transitory invasions of non hemolytic streptococci

We have had an opportunity of observing some of these remarkable cases at least five of which have been noted in earlier publications Such a mild infection may occur in an individual who presents no evidence of a previous attack of the disease and who may or may not be the subject of an old valvular affection On the other hand it may occur in a patient who has for some time presented the clinical picture of the bacteria free stage just as a more severe type of infection may take place in such an individual We will most likely find such mild forms as recurrences in patients who have suffered an attack of the disease of a more severe type and who have made a complete recovery

In these mild cases the rectal temperature may not rise to over 99 6° F for weeks at a time It may reach 101° F and rarely 10 F The patients often are up and about and may perform the duties of their occupation and take part in social activities Embolic features are not

Nearly all of the mild cases that we have recognized have recovered We can say nothing definite concerning the pathological changes in them In the course of anatomical studies of hearts however one sees lesions of small extent which may very well represent the healing of mild infections As already indicated they may be responsible for some of the bacteria free cases especially those in which embolism is not a real feature and in which the lesions in the heart are found to be moderate in extent We do not know how much myocardial insufficiency may arise in these mild cases due to myocardial lesions Nor do we know to what extent partial glomerular lesions occur nor how often a diffuse glomerular lesion may be a sequela

THE BACTERIA-FREE STAGE

It is important to distinguish between recovery and the bacteria free stage These terms introduced by one of us (E L) some years ago are arbitrary The former term was applied to cases in which the infection disappears as well as all clinical phenomena except those of any valvular defect that might have been present The term bacteria free refers to cases in which the patients have lost the infection and suffer from sequelae These sequelae as we will point out are apt to be serious in nature Under the heading Prognosis we will go more fully into the *question of recovery*

The sequelae which are characteristic of the bacteria free stage are essentially as follows renal insufficiency due to subacute or chronic glomerulonephritis progressive anemia a striking splenomegaly and embolic accidents including although rarely embolic aneurysms These aneurysms which cause the usual symptoms may be the result of healing of mycotic aneurysms developed in the bacterial stage of the disease or may arise rarely in the bacteria free stage from traumatism of the vascular wall by pieces of calcified vegetation We have evidence that leads us to believe that hepatic cirrhosis occasionally may eventuate in the cases that present a great splenomegaly

These cases of subacute bacterial endocarditis in the bacteria free stage are not rare Of the first 8 cases of subacute bacterial endocarditis studied after 1910 when we first recognized the bacteria free stage 18 or *over one fifth were in this stage The figures possibly may be still larger because this condition was not generally known and still is not and the* cases in the wards which were drawn to our attention were mainly those that had positive blood cultures and fever We are convinced that a careful study of all the cases of chronic valvular disease seen in the hos

November	30	1923	negative
December	18	1923	12 colonies to the c c
December	25	1923	20 " " " "
January	5	1924	38 " " " "
"	21	1924	12 " " " "
"	29	1924	35 " " " "
February	8	1924	25 " " " "
March	18	1924	1 " " " "
"	27	1924	2 " " " "
May	9	1924	200 " " " "
June	16	1924	18 " " " "
"	25	1924	50 " " " "
February	4	1925	8 " " " "
April	17	1925	positive only in modified Smith Noguchi medium

This patient made a complete recovery and is quite healthy at the present time January 1941 His hemoglobin for many years has been over 100 per cent In 1928 three years after the termination of his illness the murmur of the aortic insufficiency which was present all through the disease was audible no longer Apparently the scarring due to healing of vegetations narrowed the orifice

We were much surprised at the observations made on this patient especially in finding a figure as high as 200 colonies to a c c of blood at a time when he was up and about feeling well and having a temperature of only 99 2° F

It is hardly necessary to dwell upon the significance of these mild infections which we suspect occur frequently Henceforth we must entertain the possibility of the presence of this disease in patients suffering from the mildest subfebrile conditions which cannot be easily explained In patients who are the subjects of old valvular lesions this consideration is most important As blood cultures may be positive when the elevation of the temperature is trifling it will be of value to make them in patients suffering from valvular defects or congenital cardiac disease when they do not look well appear anemic or unusually tired or exhibit a change in the color of the face Only by means of such investigations will we be in a position to ascertain the real frequency of subacute bacterial endocarditis and its influence on valvular disease Such studies will be of less importance in patients who already present evidences of marked myocardial insufficiency or who have developed auricular fibrillation because we know from clinical and pathological studies that the disease is not apt to attack them

base of the vegetations to heal This was described by Osler even in acute bacterial endocarditis We speak of bacteria free cases and state whether in a given case the lesions are healing or healed The healing process even when apparently entirely accomplished often is unsatisfactory because large calcific masses may result and pendulous vegeta

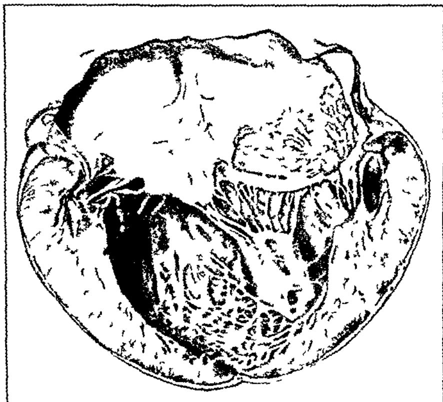


Fig 10 Subacute bacterial endocarditis bacteria free stage healed healed lesions of wall of left auricle (shark skin appearance) chordae tendineae of anterior flap torn ruptured fibrosed and calcified clinical picture was that of valvular disease and uremia

tions and bits of torn chordae tendineae may be whipped off Such calcification tends to be most marked in the aortic valve

Endocardial vegetations are present in the same locations as in the active stage of the disease (Fig 10) For a fatal case to be considered in the bacteria free stage it must be demonstrated at autopsy by means of stained spreads and sections that the vegetations are free from bacteria Cultures of vegetations alone are misleading because nonhemolytic strep-

pital during that period would have resulted in unearthing a larger number of such cases It is only by a careful scrutiny of all cases supposed to be instances of uncomplicated chronic valvular disease that one becomes impressed with the frequency with which patients are found suffering from chronic valvular disease plus subacute bacterial endocarditis in the bacteria free stage

The clinical phenomena in this stage of the disease are due to the damage done to the kidneys and the hematopoietic organs during the bacterial stage and to embolism due to the fibrous and calcareous vegetations resulting from the healing process The dark brown color of the face to be described later may well be a result of the damage to the hematopoietic organs In a case in the bacteria free stage recurrence of infection may take place occasionally Complement fixation tests made with the serum of the patients and nonhemolytic streptococci from patients in the active stage were found negative It is to be hoped that some method of immunological diagnosis may become available

It is to be stressed that repeatedly negative blood cultures in a case of subacute bacterial endocarditis do not necessarily indicate that infection is absent from the valves Blood cultures are indeed negative in cases in the bacteria free stage but negative blood cultures are obtained also occasionally in the ordinary or active cases The reasons for the negative results in the two groups are fundamentally different The cultures are negative in the bacteria free stage because there are no longer any bacteria on the surface of the endocardial vegetations so that none appear in the blood stream In the active cases on the other hand bacteria are present in large numbers on the surface of the vegetations but nevertheless blood cultures may be negative The explanation usually given is that few bacteria are disseminated into the blood stream at the time the blood culture is taken or that the blood culture technic is not good enough In the active cases theoretically and ideally blood cultures repeated often enough will reveal sooner or later the causative organism in the bacteria free stage none will be obtained However it must be remembered that even in ordinary cases of valvular heart disease without bacterial endocarditis a transient blood stream invasion may give positive blood cultures in fluid media only in about 5 to 10 per cent of cases We have seen such a transitory invasion in a case in the bacteria free stage

Pathology of Bacteria free Stage

Heart — In our discussion of the pathology of the disease in its bacterial stage we have noted that there is a strong tendency for the

in the myocardium which we have noted in the heart and aorta are in brief as follows in left auricle small or large patches of thickening of endocardium mitral valve irregular fibrotic thickening calcific deposits (Fig 13) and aneurysm of its aortic flap with or without perforation of chordæ tendineæ tearing more or less ulceration fusion knotting of



Fig 14 Subacute bacterial endocarditis bacteria free stage extensive lesions almost completely healed of bicuspid aortic valve ulceration and perforation of larger cusp and fibrosed vegetations

papillary muscles fibrous patches on the surface especially at the tip in left ventricle patches of thickening of endocardium aneurysm in position of membranous septum rarely perforation in that location of aortic valve more or less ulceration fibrous thickening calcific impregnation projecting calcareous masses (Fig 14) and of aorta aneurysm of the sinuses of Valsalva and probably narrowing of the orifices of the coronary arteries

To this appearance Gross has given the name spongy lesion (Fig 12) When these lesions are found in calcified tissue they sometimes have the appearance to which he gave the name liver lime' The "spongy lesion and the liver lime lesion have a strikingly characteristic appearance

Because of the occurrence of healing in subacute bacterial endocar

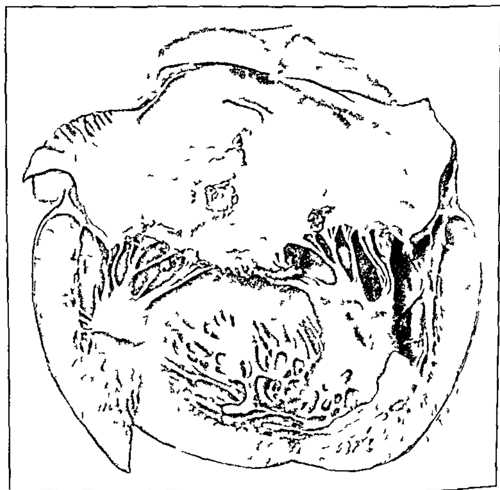


Fig 13 Subacute bacterial endocarditis bacteria free stage almost healed lesions of left auricular wall mitral valve and chordæ tendineæ fibrosed and calcified

ditis it is important to take up the subject of the effects of the disease on the valves themselves There is an abundance of evidence proving that marked changes for the worse not infrequently are induced in previously existing valvular defects and there are observations also which indicate that valvular defects may be initiated The results apart from changes

which they believe to be the result of healing of the disease While they have not advanced confirmatory evidence in the way of healed partial glomerular lesions their opinion seems to be correct The lesion of the commissures which is of the greatest interest is that type in which there is marked fibrous fusion of the flaps to each other and directly or nearly directly to the wall of the aorta Such lesions are surprisingly frequent in the aortic valves of hearts which were considered formerly to present only the lesions of rheumatic endocarditis or of atherosclerosis combined with more or less marked fibrosis and often extensive calcification Fusions of the cusps due to rheumatic endocarditis are of a different kind It is advisable that all hearts which are the seat of valvular disease especially of the aortic valve be examined with reference to the various factors concerned in the pathogenesis of such lesions Apart from the rôle which these commissural lesions play in the development of aortic valvular defects they afford additional evidence of the great frequency of healing of the lesions of subacute bacterial endocarditis

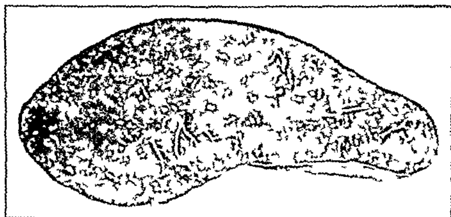


Fig 16 Subacute bacterial endocarditis bact [illegible] f [illegible] tag part of spleen with characteristic hyperplasia of pulp and Malpighian bodie

Kidney — In the bacteria free stage infarcts may be found but they are much less numerous than in cases in the active stage The partial glomerular lesions are to be found nearly always but they are few in number and entirely healed The diffuse glomerulonephritis is of particular interest because it is so much more common than in the active cases Apparently in some cases at least this develops after the febrile disease has run its course as has been found to be the case in scarlet fever and streptococcus throat infections and is considered to be of toxic (allergic) origin

The important lesions are those of the mitral cusps the chordæ tendineæ and the aortic valves These may lead to increased insufficiencies and obstructions

Of significance in this connection are the lesions of the commissures of

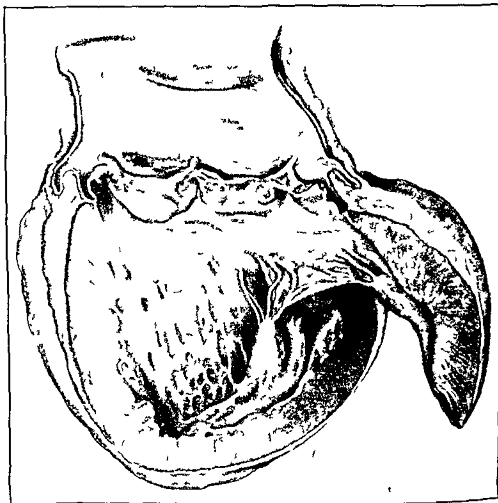


FIG 15 Subacute bacterial endocarditis peculiar lesions of the aortic valve encountered in the healed stage there is also present a typical commissure lesion at the junction of the right and posterior cusps and right and left cusps in this case there was no previous history of any attack of the disease and the patient did not present any of the features of the bacteria free stage

the aortic valve the presence of which was studied particularly by Sir Thomas Lewis (Fig 15) In the valuable paper of Lewis and Grant dealing with the relationship of bicuspid aortic valves to subacute bacterial endocarditis there were illustrations of marked forms of such lesions

General Symptoms

The bacteria free stage is an essentially afebrile condition However fever may occur as a result of complications such as embolization the breaking down of large splenic infarcts in the presence of severe anemia (anemic fever) or with the development of intercurrent infections such as pneumonias which are frequent terminally Embolism may cause fever and occasionally a chill even though there are no bacteria in the fragments broken off from the valves This has been proven experimentally by Bock In many cases the temperature is practically normal almost throughout the entire period of observation

Chills sweats and loss of weight are not characteristic of the bacteria free stage of subacute endocarditis as they are of the bacterial stage of the disease as has been noted already in this chapter

Valvular Lesions

In every one of our cases there was evidence of an organic lesion of the mitral or aortic valve often of both As a rule no new murmurs develop during the bacteria free stage of the disease but the murmur of an organic lesion may disappear

Renal Phenomena

This subject is very important in connection with the symptomatology of the bacteria free stage of subacute bacterial endocarditis but it is possible to give only the shortest account of our observations Macroscopically hemorrhagic urine usually occurs when the patient comes under observation shortly after the bacterial stage is ended or it may be a result of gross embolic lesions of the kidney or perhaps of purpura Erythrocytes in small numbers are found in the urine in a number of cases but not with the regularity or persistence with which they are found in the bacterial stage of the disease

Albumin and *casts* are found in some of the cases from time to time In others there is definite evidence of a more or less marked progressive disease of the kidney In this latter group of cases there are two types In the one there is passed a subnormal normal or increased quantity of urine of a normal or subnormal specific gravity albumin and formed elements being more or less conspicuously present The second type of case is very remarkable There is passed a large daily amount of urine

Spleen — The spleen invariably is enlarged sometimes extremely so ' There is marked congestion Infarcts are found very much less commonly than in the active cases A finding not present in the active stage is a striking hyperplasia of the Malpighian bodies and the pulp which gives the spleen a characteristic appearance (Fig 16) Microscopically the spleen in the bacteria free stage differs from that in the active stage not only in the greater hyperplasia of the lymphoid follicles but occasionally also in the presence of a focal or diffuse fibrosis of the fibrillar reticulum

Bone Marrow — The bone marrow has been studied in but few cases but in them marked regeneration was demonstrated

Clinical Features of Cases in the Bacteria free Stage

Previous History

In one case there was a history of scarlet fever at an early age In a number of cases there was a history of previous attacks of rheumatic fever and of the establishment of a valvular lesion In a few instances there was a history of an attack of fever pains in the joints palpitation and dyspnea a number of months before the development of the symptoms for which the patient came under observation It is proper to suspect that these attacks in some instances represented the bacterial stage of the disease As a rule however there is no history of the active stage of the bacterial endocarditis Occasionally patients have been observed in the active stage of the disease who while under observation pass into the bacteria free stage

Mode of Onset

In most of the cases the early symptoms are cardiac in nature There are dyspnea palpitation and cough with or without hemorrhagic expectoration With these symptoms there may or may not be chilly sensations fever sweats joint pains and swelling of the legs In one case severe pain in the thigh was the first symptom this was due to an embolic aneurysm of the femoral artery In another a severe pain in the sacral region was the prominent early symptom this is at times observed also in the bacterial stage of the disease Vomiting associated with headache and dizziness was the initial symptom complex in two cases in one case epistaxis and in another purpura first appeared Frequency of urination was a striking symptom that appeared early in two additional cases

broken off at such times On one occasion he developed a sharp chill and a rise of temperature to 104 F In the absence of any other cause it was suspected that a large piece of calcareous material had broken off The patient was observed carefully to learn where it had settled Some hours later he complained of pain in the left iliac region and the iliac

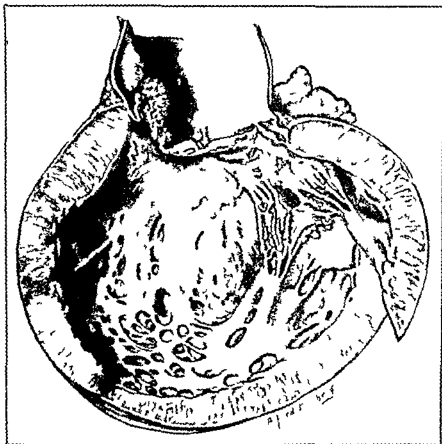


FIG 17 Subacute bacterial endocarditis bacteria free stage large calcareous mass on left cusp of aortic valve small healed lesions on other cusps tridentate fibrous area on wall of ventricle adjacent to aortic cusp of mitral valve healed lesions of chordæ tendineæ aneurysm of mitral valve no evidence of active inflammation this patient also suffered from embolic aneurysm of the left external iliac artery due to the impaction of a piece of lime from the aortic valve note also the lesion of a commissure

artery was found tender Under our eyes a large aneurysm developed The patient later died of a cerebral embolism

At the necropsy we found an aneurysm of the iliac artery and

Pains and Joint Symptoms

Diffuse pains are unusual compared with their frequency in the bacterial stage of the disease When present usually they are situated about the joints

Joint symptoms are far less common than in the bacterial stage There may be joint pains or slight joint swellings or both One must keep in mind the possibility of intercurrent rheumatic infection Occasionally the joint pains are associated with purpura Any joint swellings are as a rule slight and are transitory We do not remember having seen any joint that was tender or over which the skin was red

Aneurysms

Apart from the occurrence of aneurysms of the mitral valve the septum membranaceum and the sinuses of Valsalva which produced no recognizable symptoms there was encountered in one case an embolic aneurysm of the femoral artery The aneurysm had erupted into the soft parts and had eroded the bone A diagnosis of osteomyelitis was made because of the rapidly developing large tender swelling the fairly high temperature and the high leucocyte count with polynucleosis but it was suspected that the patient was suffering from subacute bacterial endocarditis because of the presence of a valvular lesion, a very large spleen and severe anemia The postmortem examination corroborated the latter diagnosis The vegetations were organized and bacteria free except for one minute area This was in keeping with the fact that the three blood cultures made in the case gave a negative result We believe that in this case the aneurysm was produced during the active bacterial stage

Another interesting aneurysm of the iliac artery was proven to be due to impact As far as we know this is the only proven example of such a condition since claims were made for its existence by Tufnell and Ponfick The patient a male adult who was under observation from July 2d to August 6th 1905 was suffering from aortic insufficiency The spleen was palpable and he had a dark brown color of the face which was noted in the record but the significance of which was not recognized The lower sternum was very tender There was present a very marked thrill over the base of the heart and in the jugulum This was so intense that it was suspected that it was due to a mass of lime on the valve He was afebrile except that from time to time there developed a rise of temperature to 101° F less often to 102° F After each rise petechiae were found and it was suspected that bits of calcareous material were

TRANSITIONAL CASES OF SUBACUTE BACTERIAL ENDOCARDITIS

This group of cases is described only for clinical convenience because they belong essentially to the group of cases in the active stage or those in the bacteria free stage as already have been described in this chapter by us These patients come under clinical observations in different ways as recited in the following paragraphs

1 They appear with the symptoms of the active disease and with positive blood cultures The cultures soon become negative and the patient recovers completely or presents the clinical picture of the bacteria free stage

2 The symptoms of the active stage are present but the blood culture is negative The fever and other evidences of active infection disappear so rapidly that it is clear that the negative result of the blood culture was a correct finding The outcome of these cases is like that in group 1 They simply come under observation at a time still closer to the afebrile period

3 The clinical features are essentially those of the bacteria free stage but other manifestations such as usually occur only in the active stage of the disease as for example an abundance of petechiae in the conjunctival mucous membrane together with the general non toxic appearance make it appear probable that the patient was very recently in the active stage of the disease

In one case of this last kind the suspicion that the patient was just emerging from the infectious period was strengthened by the extraordinary observation made by the patient himself that his fingers had become progressively clubbed for several months but that for a short time before coming under observation the clubbing had diminished

As the patient was a tailor and judged of the changes which were taking place in his fingers by the increasing and decreasing ability to wear his thimble we readily credited his statement The postmortem examination revealed some lesions which were in part still bacterial but many more that were bacteria free We do not know how often or to what extent recession of clubbing occurs after the infectious stage of the disease has passed For the present we must make use of this symptom cautiously for the diagnosis of subacute bacterial endocarditis because it may be the result of an earlier attack or be due to another cause Definite knowledge that the increase in size of the terminal phalanges is recent is of much value

disease we must take for granted the existence of cases in which the patient has suffered from an unrecognized infection of the endocardium and has recovered without any sequelae Such patients might remain well indefinitely except for the consequences of a previously existing valvular defect modified or not by attacks of subacute bacterial endocarditis or of valvular changes produced by the latter As already pointed out by us we do know that a patient who is apparently in the bacteria free stage suffering from certain sequelae of the previous infection may develop a recurrence the outcome of which may or may not be favorable

There is another interesting consideration to be kept in mind with regard to these cases Some of these patients as already stated die with a splenomegaly and a progressive anemia In most splenic diseases in which the patients develop anemia and perhaps cirrhosis of the liver the course of the disease is very long often lasting for decades We know that patients in the bacteria free stage having this symptom complex may pass away within a period as short as two or three years The opportunity therefore is given by these cases for making a study of the processes involved in such cases in their early stages as is otherwise not obtainable Herein lies another reason for an intensive study of the subject

Diagnosis of the Bacteria free Stage

The diagnosis of the bacteria free stage of subacute bacterial endocarditis is suggested whenever a patient with valvular heart disease presents certain other features which are not part of ordinary valvular disease These additional features are (1) renal insufficiency (2) severe progressive anemia (3) emboli (4) striking splenomegaly (5) brown pigmentation of the face

Some of these features may be observed also in active cases but unlike the latter patients in the bacteria free stage as stated above are not apt to be febrile and they do not look toxic The absence of fever for long periods and the negative blood cultures are characteristic of the bacteria free stage An important error in diagnosis is to confuse these cases with instances of chronic rheumatic valvular heart disease without recognizing the additional presence of subacute bacterial endocarditis in the bacteria free stage Cases of chronic valvular heart disease should be subjected to very careful review whenever there are present any of the features described above for which there is no other satisfactory explanation

endocarditis there were times when he ran slight elevations of temperature for a period of days at a time Some time after the second attack a tonsillectomy was performed after which there were no rises in temperature which could have been suggestive of very mild attacks

Prognosis of Subacute Bacterial Endocarditis

The outlook for patients with subacute bacterial endocarditis has been drastically and happily modified by the advent of penicillin In the original writing of this section it was deemed important to present detailed data regarding the percentage of instances of spontaneous recovery from the usual type of subacute bacterial endocarditis (Fig 19) This was necessary because for many years it was believed that the disease was always fatal In 1912 Libman pointed out that this view was incorrect and that in the first 150 active cases which he observed between 2 6 per cent and 3 6 per cent had recovered spontaneously Subsequently the writers put the figure for spontaneous recovery at 3 to 4 per cent one of us (E L) having personally observed at least 25 such cases

The likelihood that 3 to 4 per cent of active cases of subacute bacterial endocarditis could recover spontaneously assumed additional significance when claims of curative effects were made for various therapeutic measures In a series of cases reported by different observers to have been treated by sulfonamides with and without heparin or fever therapy the recovery rate averaged 5 5 per cent This was not strikingly better than the control figure of 3 to 4 per cent further more these cases included series with unusually high recovery rates which were too small to be acceptable as statistically valid

Prior to the use of sulfonamides some recoveries were not likely to be reported because with recovery of the patient the observer came to doubt his diagnosis But when recovery followed sulfonamide therapy the cure was readily attributed to the drugs used and the case was likely to be reported Even with allowances for these considerations it seemed apparent to us that with sulfonamide therapy there was a small but definite increase in the number of recoveries from subacute bacterial endocarditis An even more encouraging feature of sulfonamide therapy was the frequency of temporary remissions especially when the patients were treated with massive doses of sulfonamides This suggested that a more potent chemotherapeutic agent which could be given in large doses without the toxicity which resulted from sulfonamides would be effective in curing the disease

The administration of penicillin in appropriate dosage has transformed the prognosis from almost complete hopelessness to one of expected recovery in a large majority of the cases At present the few series of reported cases of subacute bacterial endocarditis treated with penicillin are too small to permit an accurate estimate of the percentage of recoveries that may be anticipated

Case 5 — 1923 1924 Patient was observed first April 5 to 8 1923 He was clearly in the bacteria free stage He had a very large spleen the characteristic dark brown pigmentation of the face and was afebrile He was in the hospital again from May 12 to 31 1924 The spleen still was large there was clubbing of the fingers petechiae anemia and fever He again returned on October 17 with the same symptoms and Osler lesions The blood culture was positive A few days later many 13 5 per cent macrophages were found in the blood The patient died on November 7 1924 The length of the interval was not clear but was something under thirteen months At the postmortem examination there were found healed lesions and also fresh lesions The spleen was enormous and showed the marked hyperplasia of the bacteria free stage The kidneys presented two sets of embolic lesions the one completely healed the other recent Note This patient came under observation in the bacteria free stage developed a second attack and died

Case 6 — 1923 1924 1925 Mild case The patient came under observation in the bacteria free stage The duration judging by the history as regards anemia and weakness was at least seven months The blood cultures were negative There were intense anemia marked splenic enlargement and moderate fever The diagnosis of the bacteria free stage was confirmed by the prompt disappearance of the fever (anemic fever) following transfusion The patient was in the hospital again from June 13 to July 21 1924 Anemia and splenic enlargement still were present There was no evidence of active infection The patient was admitted again on January 18 1925 There were fever petechiae and the splenic enlargement had increased Two blood cultures were positive The patient left the hospital on March 11 1925 with the spleen still enlarged On May 25 the spleen was no longer palpable The hemoglobin now was 88 per cent it had been 34 per cent in January 1924 68 per cent in April 1925 During July and August there were slight elevation of temperature and positive blood culture The patient was practically well from September 1925 She was traced until 1932 and there were no new developments Note The patient came under observation in the bacteria free stage and then had a second attack after which the splenic enlargement disappeared There was a third attack with recovery

As a result of these and other studies the following forms of recurrence may be described (1) an attack of infection a period of good health, a second attack followed by good health (2) same as (1) but the second attack being fatal (3) an attack of infection symptoms of the bacteria free stage followed by a second attack with fatal outcome (4) symptoms of the bacteria free stage followed by an attack of the active disease with fatal issue (5) symptoms of the bacteria free stage another attack of infection symptoms of the bacteria free stage persisting

The sixth case is of particular interest because it is the only one in which we have observed a patient in the bacteria free stage who after another attack of infection completely recovered In the third case the patient had repeated tonsillitis and besides the two major attacks of

endocarditis there were times when he ran slight elevations of temperature for a period of days at a time Some time after the second attack a tonsillectomy was performed after which there were no rises in temperature which could have been suggestive of very mild attacks

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Nevertheless active bacterial infection appears to have been eliminated in 75 to 85 per cent of the cases

In a total of 131 cases reported by 6 different groups of observers cure of the bacterial infection was achieved in 107 cases or 81 7 per cent In the largest single series of 62 cases reported by Loewe bacterial sterilization occurred in 50

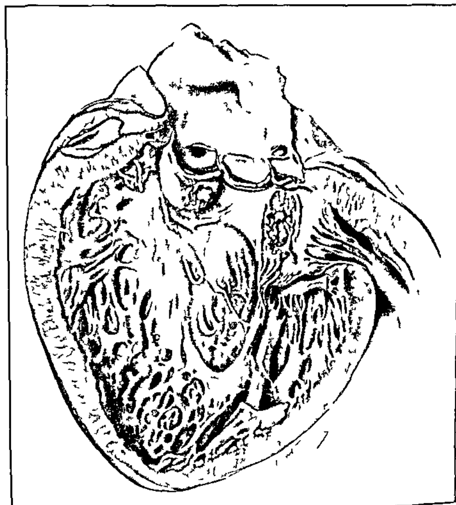


Fig 19 Subacute bacterial endocarditis recovery death 8 years later from heart failure due to repeated attacks of rheumatic fever ballooning of right aortic cusp large calcified mass in back of right cusp visible through perforation of this cusp small multiple calcified lesions on ventricular aspect of cusp extending to subjacent mural endocardium large ulcerated area of anterior flap of mitral valve with ribbing due to traumatism from the protruding mass of lime in right aortic flap small vegetations of terminal attack of acute staphylococcus endocarditis in center and lower margin of eroded area

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92 per cent of 12 patients recovered after penicillin therapy including all of the last 11 treated In fact the percentage of cures would probably be higher if some of the cases were excluded which were inadequately treated in the early period of the penicillin era either because of lack of knowledge of the necessary dosage or because of the inadequacy of the penicillin available

On the other hand these reports do not include cases in which the causative organism was other than a non hemolytic streptococcus and some cases due to non hemolytic streptococci which appeared to be too resistant to penicillin in vitro In some instances recovery from the infection was impaired by congestive heart failure which developed during treatment or which had appeared before treatment was begun and persisted despite bacteriological cure In a number of cases death from heart failure or embolization occurred despite the fact that previously positive blood cultures had become negative during treatment and that postmortem studies indicated that the bacterial vegetation had been healed

Certain factors which appear to influence the outcome in cases of subacute bacterial endocarditis may now be listed tentatively

Sensitivity of the Organism to Penicillin — Non hemolytic streptococci the causative organisms in more than 90 per cent of the cases of subacute bacterial endocarditis usually are somewhat more resistant to penicillin than other gram positive or gram negative cocci However it is relatively easy to obtain blood levels of penicillin which are considerably higher than the concentrations necessary to sterilize in vitro most cultures of the non hemolytic streptococci However some of the non hemolytic streptococci are relatively more resistant than others in particular the variety known as enterococcus is often 8 or more times as resistant as most non hemolytic streptococci

Several observers have commented that the more sensitive the causative organism the more likely and more prompt the response to penicillin therapy and the more favorable the prognosis This correlation is imperfect and applies only in a limited sense In general sterilization of the infection may be anticipated when the resistance in vitro of the non hemolytic streptococcus is not more than 4 times that of a standard hemolytic streptococcus or staphylococcus However other factors may result in a fatality even when the causative organism is very sensitive to penicillin And conversely with the massive doses of penicillin now available cases of subacute bacterial endocarditis due to relatively resistant organisms may possibly be cured In fact within the group of sensitive non hemolytic streptococci the degree of sensitivity or resistance appears to be more of a guide to the dosage of penicillin needed than to the prognosis For except in cases due to organisms which are entirely insensitive or very resistant to penicillin it is possible to attain concentrations of penicillin in the blood which greatly exceed that required to sterilize these organisms in vitro Whenever such adequate levels can be achieved and maintained continuously for periods of

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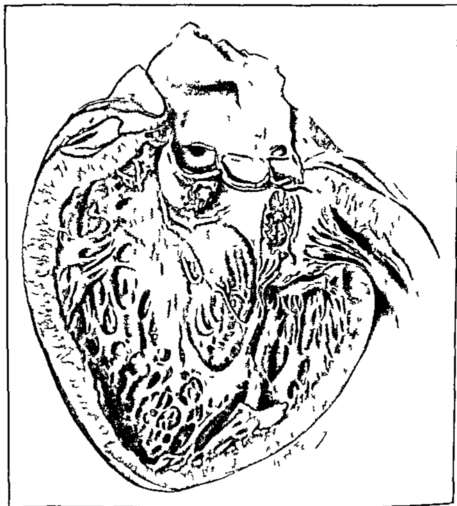


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because of the danger of fatal cerebral or coronary embolism or occasionally be cause of suppuration of a visceral infarct When there is extensive ulceration and destruction of valvular tissue *there appears to be great difficulty in sterilizing the bacterial vegetations and some of the treatment failures have been attributed to this cause* Occasionally ulceration is followed by infection of the pericardium and the development of a fatal pericarditis Destruction of valvular substance by aggravating a previous valvular deficiency or adding a new one may contribute also to heart failure even when the infection is cured

Age and Sex —The prognosis does not appear to be significantly modified by the age or sex of the patient

Underlying Disease —Recoveries have been effected with equal frequency whether the underlying disease was rheumatic or congenital

Cause of Death in Subacute Bacterial Endocarditis

In cases which are not cured by penicillin or other therapy death occurs *in the vast majority of them in about 14 to 18 months after the onset of the disease When patients succumb despite penicillin therapy* cardiac failure appears to be an earlier complication and a more frequent cause of death than before the advent of penicillin In such cases the most frequent condition leading to a fatal outcome is exhaustion The myocardial weakness that may be present usually is of the type due to fever anemia and general weakness Sudden closures of cerebral arteries and intracerebral subarachnoid and intraventricular hemorrhages often are the final events Pulmonary edema frequently is an accompaniment Very frequent causes of death are embolisms in various parts of the body and uremia In cases of mitral stenosis death may occur with the usual symptoms of rapidly increasing cardiac failure preceded or not by hemoptysis due to pulmonary infarction or apoplexy and terminating with pulmonary edema At times death is due to large vegetations *acting like a ball valve thrombus and occluding the orifice In a certain number of instances an intercurrent pneumonia cuts short the disease* Rupture of mycotic aneurysms not infrequently leads to a rather sudden termination Occasionally a miliary tuberculosis of the lungs or general miliary tuberculosis or some other intercurrent or preceding disease may shorten the patient s life Hyperpyrexia is a rare cause of death Unusual causes of death are embolisms of the left or right coronary artery Perforation of the infarcted myocardium may result A number of other causes of death have been mentioned throughout the text

Among the causes of sudden death are two cases of particular interest The first patient (West) had not been at all ill While playing tennis he felt sick became unconscious and died practically instantly *At the necropsy there was found an embolism at the bifurcation of the left coronary artery* occluding both

3 to 6 weeks or longer, one can expect that recovery will ensue provided treatment has been begun early in the disease, and provided no serious complications occur before treatment is completed

Certain uncommon causes of subacute bacterial endocarditis such as the influenza melitensis proteus and other gram negative bacilli are so resistant to penicillin that it is impossible at present to obtain blood levels of penicillin adequate for sterilization of the bacterial vegetations The favorable figures for recovery with penicillin, quoted above, do not apply to cases due to these organisms Occasional spontaneous recoveries have been observed, and in a few instances recovery from subacute influenzal endocarditis has been attributed to the use of sulfonamides When streptomycin becomes available in generous quantities one can at least expect that the percentage of recoveries in cases due to gram negative bacilli may be found to be much large than now

Duration of the Disease before Treatment — The outlook for recovery grows poorer the longer the period of infection prior to treatment with penicillin but many exceptions occur due to great variation in the progress of the disease and the development of complication in individual cases One of Loewe s recovered patients was ill almost a year before penicillin therapy However, the same observer obtained the most favorable results in cases in which the duration of the disease was less than three months With the passage of time the valvular vegetations are likely to grow larger, ulceration of the valve occurs, new valvular or other endocardial regions are involved and potentially fatal emboli and arterial aneurysms are likely to develop All these extensions or complications of the disease enhance the difficulty of eradicating all of the bacteria with penicillin and consequently diminish the likelihood of cure It is apparent that early diagnosis and the prompt institution of penicillin therapy in adequate dosage by avoiding these complications improve the prognosis for recovery

General Condition of the Patient — Deterioration of the patient's general condition as manifested by severe emaciation, asthenia and anemia may lead to a fatality before adequate penicillin is administered or it may interfere with recovery even when the bacterial infection can be controlled On the other hand extreme weight loss and prostration in themselves are not incompatible with recovery Often there is an almost miraculous improvement in the patient s previously deteriorated general condition as soon as the infection is neutralized

Presence of Complications — Certain complications of subacute bacterial endocarditis suggest an unfavorable prognosis for they may prevent eradication of the infection and may cause sudden death or they may lead to invalidism or death even when the infection itself is eliminated Heart failure may develop before or during treatment with penicillin or when activity is resumed following treatment Death from heart failure may interrupt penicillin therapy or nullify a bacteriological cure Similarly repeated embolization is an unfavorable sign

prophylactic dosages for both intramuscular and oral penicillin therapy remain to be established

A convenient time for a search and eradication of foci of infection is toward the end of penicillin therapy for an established bacterial endocarditis Infected teeth may be extracted tonsils removed or sinus infections treated while the patient continues to receive full doses of penicillin In these cases infected foci are eliminated in order to prevent a recurrence of bacteremia and bacterial endocarditis In a number of cases it has been apparent that fever and other signs of infection which confuse the clinical course of bacterial endocarditis with penicillin therapy were due to active dental infections or acute tonsillitis For this reason it appears desirable and sometimes it is essential that definitely infected teeth and tonsils be removed as early as possible during penicillin therapy as the condition of the patient permits in order to prevent interference with a satisfactory therapeutic response of the major disease

Treatment of Subacute Bacterial Endocarditis

The discovery of penicillin and its successful application to the treatment of subacute bacterial endocarditis have relegated all other therapeutic measures to a minor place Current reports although involving relatively small series of cases appear uniform in indicating that 80 per cent or more of the cases of subacute bacterial endocarditis can be cured of bacterial infection by means of penicillin therapy This applies to those instances of the disease due to non hemolytic streptococcus the causative organism in over 90 per cent of the cases It is likely also that similar favorable results are obtainable in the relatively rare cases due to other gram positive organisms or gram negative cocci Penicillin is not effective in cases due to gram negative bacilli but streptomycin is effective for some of these

Penicillin Therapy[199-208]

Sensitivity of Causative Organism — It is essential that the clinical diagnosis of subacute bacterial endocarditis be confirmed bacteriologically by identification of the causative organism with the aid of blood cultures This is necessary both to avoid useless treatment with penicillin when the organism is completely resistant and to determine the degree of sensitivity of those causative organisms which are susceptible to penicillin For even among the susceptible organisms variations in penicillin sensitivity or resistance are sufficiently great to necessitate corresponding variations in the dosage of penicillin required

The sensitivity of the causative organism is determined in vitro by some modification of the Oxford cup test or more commonly by some method of serial dilution in test tubes The exact technic has been described by Foster and

distal branches The aortic valve was the seat of ulceration Another case of instantaneous-death was reported by Kidd In his patient death was due to an ulceration of the conduction system A large myocardial lesion was found to have eroded through from the left ventricle into the right auricle, largely destroying the region occupied by Tawara's node Other subendocardial ulcerations intercepted the path of the left branch of the bundle of His Instant death in this patient was thought to have been due to the sudden onset of heart block followed by ventricular asystole or fibrillation

Prophylaxis of Subacute Bacterial Endocarditis

Horder was the first to suggest prophylactic measures Inasmuch as the great majority of cases are due to superadded infections of valves, which are the seat of previous rheumatic infection or congenital malformation, the broader problem becomes one of prevention of these diseases The more immediate consideration is the prevention of subacute bacterial endocarditis in patients who already have a valvular lesion or a congenital defect Cognizance should be taken of the fact that many of the patients who develop the disease were never aware of a previous valvular lesion In other cases a valve lesion giving no symptoms was discovered accidentally often months or years before the onset of the subacute bacterial endocarditis and usually in the course of an insurance examination In another larger group the patients are aware of a previous valve lesion but the symptoms are too slight to cause them to change their habits of life As already pointed out individuals showing definite cardiac failure rarely develop the disease The problem of prophylaxis should therefore be directed particularly to the cases in which the valve lesion is causing no or but trifling discomfort

All such individuals should be kept under observation Search should be made at regular intervals for a focus of infection especially in teeth and tonsils Every possible means should be employed of improving the general resistance Emphasis must be laid on hygienic living Care of the intestinal tract has been found to be a valuable means of improving the general resistance As physical and mental strain appear to be outstanding predisposing factors in some cases they should be removed or minimized Respiratory infections should be avoided by minimizing contact with persons suffering from these infections and by avoiding climatic exposure and fatigue

The probability that subacute bacterial endocarditis may develop following the trauma of removing foci of infection especially infected teeth is justifiable reason for the administration of penicillin therapy for 48 hours before and at least 3 days after the operative procedure This applies to individuals susceptible to bacterial endocarditis because of a rheumatic or congenital cardiovascular lesion It is hoped that oral penicillin will prove adequate for this purpose Suitable

continuous intramuscular drip or by injections of penicillin in peanut oil and beeswax[41 13 91]

Continuous Intravenous Infusion — The total dosage for a 24 hour period is dissolved in not more than 1 500 c c of physiological saline or 5 per cent glucose solution or aliquot portions may be prepared for 8- or 12 hour periods In the presence of cardiac failure it is preferable to limit the total amount of fluid injected to 1 000 c c and to substitute glucose in distilled water for the saline

The solution of penicillin is administered with the aid of a gravity infusion set equipped with a glass Murphy drip chamber for observing and a screw clamp or three way stop-cock for controlling the rate of flow A 1 inch long needle of 18 to 21 gauge is connected with the infusion apparatus and inserted most of its length into a convenient vein on the dorsum of the forearm or hand or occasionally in a vein on the dorsum of the foot Whenever possible a vein should be chosen which permits free motion of the hand and arm The infusion is run continuously throughout the day and night at a slow regular rate designed to administer the desired 1 000 to 1 500 c c of penicillin solution in 24 hours

The chief advantage claimed for this method of administration is the continuous maintenance of the desired high level of penicillin When skilfully executed this method of administration permits many patients a relatively higher degree of comfort than other modes of giving the drug Most patients receiving a continuous intravenous infusion of penicillin are able to feed themselves read play cards and sleep well despite the continued and prolonged presence of the needle in a vein

However there are several disadvantages which often justify the use of intramuscular administration of penicillin *Technically continuous intravenous infusion requires much greater skill than intramuscular injection and relatively close and constant supervision* In fact any interruption of flow due to blockage of the needle or other cause unless promptly corrected results in nullification of the major advantage claimed namely continued maintenance of high serum penicillin levels For this reason continuous intravenous infusion of penicillin for the treatment of subacute bacterial endocarditis must be limited largely to hospital practice This is a distinct disadvantage and it is hoped that treatment can be so simplified that it can be started early in the disease and with the limited facilities available to the general practitioner in the patient s home

Other disadvantages associated with continuous intravenous therapy are the need for changing the complete equipment and introducing the needle into a new vein after 3 to 5 days or less *the frequent development of thrombophlebitis near the needle s site and occasionally the development of fever or chills and fever sometimes associated with any form of continuous intravenous therapy*

Intermittent Intramuscular Injections — The intramuscular injections of penicillin are given at regular intervals of 1 2 or 3 hours throughout the day and

Woodruff, Fleming, Dawson and associates 1944 and others[10] In general commercial penicillin is diluted to a weak concentration for example 1 unit per c c or $\frac{1}{10}$ unit per c c A fraction of a c c of this solution is then diluted serially with broth to make a total of 1 c c in each tube, and to give the likely range of concentrations necessary to inhibit the organism to be tested This range may include tubes containing 08, 06 04, 03, 02, and 01 units of penicillin per c c These solutions are inoculated with 1 c c of a young culture of the causative organism *After 24 hours incubation observation of the series of tubes will dis*close the lowest concentration which completely inhibits the growth of the organism This concentration represents the sensitivity of the organism For control a similar series of tubes with identical concentrations of penicillin in broth are inoculated and incubated with equal amounts of a culture of a standard organism usually a staphylococcus aureus or a streptococcus hemolyticus Since the sensitivity of the standard organism to penicillin is known this test serves also as a check on the effectiveness of the commercial penicillin being used

After penicillin has been administered the concentration of penicillin in the blood can be determined in a similar manner as frequently as is desired (Rammelkamp[10] [11] Loewe[0]) In this procedure a series of tubes containing 0 8 0 7 0 6 0 5 etc c c of serum are each made up to 1 c c with broth Each tube is then inoculated with 1 c c of a suspension of young culture of the standard organism and the whole incubated for 4 hours In this way the amount of serum necessary to inhibit growth of the standard organism is determined Since the sensitivity of the standard organism is known in terms of Oxford units per c c it is possible to calculate the number of Oxford units per c c of serum Experience and knowledge of the dosage of penicillin administered enable one to determine in advance the range of dilutions of serum to be used in the test

The standard organism employed by many observers has been found to be inhibited by an average of 0 Oxford units of penicillin per c c In comparison these observers found the penicillin sensitivity of the streptococcus viridans or non hemolytic streptococci responsible for subacute bacterial endocarditis to vary between 007 to 0 5 (Loewe[07]) 0 02 to 0 05 (Coerner and associates[04]), 015 to 08 (Mokotoff and associates[09]) 008 to 14 (Dawson and Hunter[01]) and 008 to 0 3 (Meads and associates[03]) The sensitivity of these organisms usually varied between 1 and 4 times the resistance of the standard organism to penicillin but occasionally the resistance of some of the non hemolytic streptococci e g enterococci were 20 or more times as resistant as the standard organism

Modes of Administration of Penicillin[214] [15]

The penicillin may be administered by a constant intravenous infusion (venoclysis) by intramuscular injections repeated at regular intervals by a

of being associated with more pain and of permitting the patient less freedom of motion The even regulation of the rate of flow has proved more difficult and the rate of absorption more irregular than by continuous venoclysis

Combined Methods of Administration — Sometimes it is necessary to combine two or more of the above methods of administering penicillin Treatment may be begun by continuous intravenous administration and continued for 3 weeks as recommended by Bloomfield and associates[199] and then followed by intramuscular injections every 3 hours for 3 to 5 weeks Often the shift from continuous intravenous to repeated intramuscular injections is necessitated by the difficulty in finding new accessible veins or occasional intramuscular injections may be given during intervals in which the continuous intravenous infusion becomes blocked and cannot be restored promptly Occasionally an effective penicillin blood level cannot be attained by one method as readily as by the other

It should be emphasized that since the therapeutic superiority of one method of administration over any other has not been established that method should be chosen which is most likely to be effective in terms of the available facilities the skill and experience of the physician or his assistants with that method the tolerance and comfort of the patient the ability to attain an effective blood level by the method chosen and finally all other things being equal the minimal expense to the patient

Oral Penicillin — Penicillin administered orally is largely destroyed by the acidity of the normal stomach but sufficient amounts may be absorbed to be of practical therapeutic value The highest penicillin blood levels are attained by the oral route when the penicillin is taken at least half an hour before breakfast and the levels also may be enhanced by the use of antacids buffers special capsules etc Therapeutic results attained in the treatment of gonorrhea and pneumococcic pneumonia with oral penicillin have been comparable to those achieved with intramuscular injections Preliminary observations in the treatment of these diseases indicate that 2½ to 5 times the intramuscular dose must be given orally to attain corresponding levels The large dosage required in the treatment of subacute bacterial endocarditis and the irregularity of absorption from the gastrointestinal tract make the oral administration of penicillin unreliable at the present time Furthermore the cost would be very great However the advantages of the oral route for the administration of penicillin are so obvious and the effectiveness of oral penicillin in the treatment of diseases caused by more sensitive organisms are so encouraging that it may be hoped that this route will prove both practical and effective

Dosage and Duration of Therapy — It is clear that a considerably higher daily dosage of penicillin and a considerably longer period of administration are necessary in the treatment of subacute bacterial endocarditis due to non hemolytic streptococci than in the treatment of most diseases due to the other common

night Accordingly the total dosage of penicillin for the 24 hour period is divided into 24 12 or 8 doses respectively after dilution with physiological saline so as to contain the desired individual dose in 1 to 3 c c The injections are made successively into the right and left gluteal and right and left deltoid muscles in such a way as to cause minimal injury or pain

Since it is known that relatively little penicillin remains in the blood 60 to 90 minutes after a single intramuscular injection and none after 2 to 3 hours it appears theoretically desirable not to extend the interval between injections to more than 2 to 3 hours For the maintenance of continuously high levels hourly injections are desirable as recommended and given by Mokotoff and his co workers [03] Such frequent injections require almost constant nursing attention and may be associated with considerable discomfort, when given over a long period of time However most patients become accustomed to this trying procedure There is much that is still unknown regarding the most effective distribution of dosage and intervals in the method of intermittent intramuscular injection Many patients have been cured by injections at 3 hour intervals even though there was no detectable penicillin in the blood for at least one third of the period of treatment It is unknown whether the maximum level of serum penicillin is an important factor in determining cure as well as the continuity of an effective blood level It is undetermined whether penicillin in sufficiently high doses can be effective in the treatment of subacute bacterial endocarditis even though given at longer intervals than is now recommended, for example every 4 or 6 hours With resistant strains it is conceivable that a few very large doses of penicillin at relatively long intervals may be curative when the same total dosage administered to give constant but ineffective levels is futile

The chief advantage of the intermittent intramuscular injections is the simplicity of preparation and administration of the penicillin solution The chief disadvantages are the pain and often the psychic trauma associated with the repeated injections The results of treatment thus far do not provide any conclusive evidence that the percentage of cures by this method is significantly less than by continuous intravenous infusion

Continuous Intramuscular Infusion — Penicillin may be administered in a similar manner to that described under continuous intravenous infusion except that a longer needle is inserted into a muscle instead of into a vein Such a method of continuous intramuscular infusion of penicillin has been described by Harris [0] and has been employed in the treatment of a number of cases of subacute bacterial endocarditis by Dawson and Hunter [01] Mokotoff and associates [09] and others A continuously high level of serum penicillin thus can be obtained corresponding in all respects to that achieved by continuous intravenous infusion This method has the advantage of requiring less constant attention and less technical skill than continuous intravenous infusion but has the disadvantage

The afore mentioned dosages may require considerable modification according to the sensitivity of the organism and the clinical condition of the patient There appears to be a distinct correlation between the sensitivity of bacteria to penicillin in vitro and in vivo However it is uncertain what mathematical relationship is necessary between the penicillin concentration necessary to destroy given bacteria in the test tube and the serum level of penicillin which would be effective in the destruction of these organisms in the human body According to Loewe[97] the best clinical results are achieved when penicillin is administered in dosages sufficient to maintain a blood serum level of at least 5 to 10 times that indicated by the in vitro test Goerner and his associates [1] obtained excellent results by maintaining a penicillin level of at least three times that of the inhibiting level

Experience has shown that there is considerable variation in the serum penicillin level attained with a given dose of penicillin in different individuals by different routes of administration and even in the same individual at different times It is therefore impossible to state in advance the exact dosage necessary to achieve an effective blood level of penicillin to destroy bacteria of known in vitro insensitivity But in a general way one can decide in advance that if a daily dosage of 250 000 to ,00 000 is the minimum effective dose to be employed in cases of subacute bacterial endocarditis due to a non hemolytic streptococcus whose resistance is no more than four times that of a standard organism then proportionately higher doses 500 000 to ,000 000 daily should be given from the beginning if the resistance is higher It is probable that the therapeutic results are likely to be better the sooner the effective dose is administered For this reason it is desirable not to delay adequate dosage until clinical and bacteriological observations and repeated determinations of the penicillin level of the blood point to the need for an increase of penicillin

There are undoubtedly other factors besides the resistance of the organism which may be important in determining the needed dose of penicillin Among these factors are a long duration of the illness before treatment is begun the presence of complications particularly frequent embolization and heart failure poor general condition of the patient and the history of lack of response to previous penicillin therapy These are all warnings that high or massive dosage of penicillin should be given without delay regardless of the in vitro sensitivity of the causative organism However in spite of all efforts to gauge the proper dosage in advance it may be found that the serum penicillin level attained is inadequate that the patient s clinical condition does not improve significantly or that blood cultures remain positive In any of these eventualities the dose of penicillin should be increased rapidly regardless of any theoretical considerations which indicated that the previous dose was adequate

The effectiveness of penicillin treatment in this disease is to be measured not merely by the percentage of cures obtained by a few observers working in

gram positive or gram negative cocci In many instances of subacute bacterial endocarditis cure has been achieved by a daily dosage of 200 000 units of penicillin administered intravenously or by regular intermittent intramuscular injections for a period of 2 to 4 weeks However, it is probable that a higher percentage of cures will be obtained, if therapy even in the most favorable cases is begun with a minimal dosage of 500 000 units daily A minimal daily dosage of 1,000 000 units would be even more desirable

Although the smaller dosages have proven effective in many instances it has often been necessary to raise the dosage after a week or two of treatment has failed to afford clinical or bacteriological improvement, or after a routine course of treatment was completed and promptly followed by a clinical and bacteriological relapse In most of the latter retreatment with higher doses of penicillin usually has effected a cure For this reason it might appear more economical to try the smaller doses of 200 000 to 240 000 daily and to reserve the larger doses for those patients who fail to respond However, a study of the reported failures in treatment strongly suggests that inadequate initial treatment may be an important factor in such failure Inadequate treatment may be tantamount to no treatment at all thus permitting a more or less prolonged interval during which enlargement of vegetations ulceration of valvular tissue embolization or heart failure may develop to a sufficient extent to frustrate later therapeutic endeavors with belatedly adequate dosage

The necessary *duration of treatment* has not been clearly established and probably varies considerably with the individual case While some of the early cases were treated successfully with as little as 200 000 units daily for a period of 2 weeks most workers now recommend a minimum of 3 weeks of continuous treatment However it has often been necessary to extend the period of treatment to 5 10 or more weeks in order to effect a cure As with dosage it is probably safer to accept the higher figures as the minimal initial duration of treatment than to risk the development of irreversible complications Tentatively it seems desirable to advocate a minimal dose of 1 000 000 units of penicillin daily for a period of 5 weeks a total of 35 000 000 units However a lesser dose of 500 000 units daily for 4 weeks or a total of 14 000 000 may be administered in very favorable cases of brief duration due to a sensitive causative organism and without clinical complications

It appears from reported cases that a successful result is rarely achieved with less than a total dosage of 4 000 000 units and that in a high percentage of cases more than 10 000,000 units were necessary Loewe and his co-workers [67] have administered as much as $2\frac{1}{4}$ million units daily and a total of up to 95 million units It is desirable to determine the respective importance of the daily dose and the duration of treatment and whether with sufficiently high dosage the period of treatment can be shortened

heparin are such as to restrict the treatment of the disease to specially skilled groups of physicians working in hospitals There is no justification for such limitation in view of the excellent results obtained with penicillin alone Other disadvantages of heparin include the rather frequent occurrence of fever which confuses the clinical course and the risk of hemorrhage especially cerebral hemorrhage with overdosage The hope that heparin might prevent the development of thrombophlebitis in the veins being used for continuous intravenous administration of penicillin has not been realized Dicumarol has been used instead of heparin[95] but as for heparin this has not seemed to improve results

Clinical Course with Penicillin

In favorable cases and with adequate penicillin dosage striking clinical improvement occurs rapidly Usually within a few days and sometimes within 24 hours there is a general improvement in the patient s sense of well being and an increase in his appetite and physical strength The blood culture may become negative within 4 hours and usually by the end of the first day Thereafter blood cultures should remain negative otherwise one should question the adequacy of treatment and increase the penicillin dosage With an unsatisfactory response the blood cultures may remain positive despite treatment or become positive again a few days after treatment is discontinued In either instance higher penicillin dosage and longer courses of treatment are indicated The sensitivity of the organisms should be rechecked as an additional guide to dosage As a rule the patient remains bacteriologically cured if blood cultures are negative and clinical signs of infection are absent for at least 4 weeks after discontinuation of penicillin therapy Occasional instances of recurrence after longer intervals have been noted but it is uncertain whether these cases represent relapses or reinfections

The temperature usually reaches normal levels by the end of a week s treatment However low grade fever may persist or recur after the first week even in cases resulting satisfactorily Fever may be due to the intravenous administration of penicillin and it is common when heparin is administered simultaneously Embolization usually is denoted by a spike in the temperature curve In some cases in which the bacterial infection is controlled by the penicillin persistent fever may well be due to a concomitant active rheumatic fever which may or may not be manifested by joint symptoms prolonged auriculoventricular conduction time or pericarditis A therapeutic test with salicylates is desirable and may aid in deciding whether active rheumatic infection is the likely cause of the fever As a rule persistent elevation of temperature to 101° F or higher after the first week of treatment is likely to signify unsatisfactory therapeutic response and should be considered an indication for larger doses of penicillin

large hospitals with ideal facilities but also by the widespread availability of the method of treatment to doctors everywhere As a rule, blood cultures necessary to prove the diagnosis and identify the causative organism are generally available to the practicing physician With little additional difficulty the sensitivity of the causative organism can be determined by the same laboratory While subsequent determinations of the penicillin level and repeated blood cultures may be helpful guides in therapy, difficulties in obtaining them for one reason or another do not justify delay in commencing treatment until the patient can be hospitalized in a large institution, where all these facilities are readily available It is preferable to advise that the physician begin empirically with 1 000,000 units daily given in equal divided doses by intramuscular injection every 2 or 3 hours and continue for at least 3 and preferably 5 weeks Although fever and embolization may persist during a course of treatment which is to prove effective, it seems desirable when blood cultures are not readily available to increase the dosage if there is a significant elevation of temperature or evidence of embolization after 1 week of treatment By following these guides gained from experiences thus far recorded the general physician undoubtedly will attain a high degree of success in the treatment of subacute bacterial endocarditis even when he is without the benefit of every technical and laboratory aid available in large hospitals Speed in the commencement of treatment and large initial doses should compensate for most of the disadvantages

Adjuvants to Penicillin Therapy

In some cases effective penicillin levels are difficult or impossible to attain either because of the resistance of the organism or because of too rapid excretion of the penicillin To enhance the blood level achieved by a given dose of penicillin other substances have been administered simultaneously which by competing for excretion through the renal tubules have slowed the excretion of penicillin Para amino hippuric acid[200] and diodrast have been used for this purpose and actually have permitted the development of a higher penicillin level It is uncertain whether these substances will prove of frequent practical benefit for penicillin can now be given in huge doses without toxicity, and these large doses in themselves impede tubular excretion

The anticoagulant heparin has been employed also by a number of observers [97, 19] to promote the effectiveness of penicillin therapy, just as it had been used previously in combination with sulfonamides While there may be theoretical reasons for its use nearly all observers agree that the favorable therapeutic results obtained with penicillin alone are quite as striking as those achieved with the aid of heparin The more complicated set up necessary when heparin is used the need for frequent determinations of the coagulation time and the cost of the

the probability of irreversible damage increases with each day that the infection is not controlled

Heart failure may prevent a satisfactory therapeutic result either by causing a fatality before adequate penicillin can be given or by causing extreme disability or death after bacterial sterilization has been accomplished To a large degree heart failure is the consequence of the underlying cardiovalvular disease and to persistent or recurrent rheumatic activity However the bacterial endocarditis may precipitate or contribute to the development of heart failure by adding the strain of infection by increasing the valvular and myocardial damage or by producing embolisms To the extent that the heart failure is the consequence of the bacterial infection its prevention and control are dependent upon the promptness with which penicillin is given in adequate dosage At the same time of course restriction of salt and fluids digitalization and the administration of diuretics are additional therapeutic measures to be employed as with heart failure due to other causes

Other Forms of Antibiotic Therapy and Chemotherapy

Streptomycin [illegible] — Subacute bacterial endocarditis sometimes is caused by bacteria not susceptible in vitro to penicillin but susceptible to streptomycin Among these are *Streptococcus fecalis Escherichia coli Aerobacter aerogenes Hemophilus influenzae Klebsiella pneumoniae Brucella Pasteurella pestis Pseudomonas aeruginosa* and others When any one of these organisms is found causative of subacute bacterial endocarditis such a patient should be given streptomycin intravenously or intramuscularly in unit dosage equivalent to the large doses recommended for penicillin Like penicillin streptomycin has low toxicity for man

Sulfonamides — When the antibiotics are ineffective because of the high resistance of the causative organism sulfonamides should be given a therapeutic trial There were insufficient observations to permit a conclusive evaluation of the effectiveness of the sulfonamides when these drugs were almost entirely replaced by penicillin in the treatment of subacute bacterial endocarditis Long had observed 4 per cent recoveries in 120 cases treated with sulfanilamide a figure not significantly greater than that which we have accepted tentatively for spontaneous recovery However we had the distinct impression that somewhat more cases were recovering following the use of sulfonamides than had previously been noted

Some workers claimed better results from the combination of sulfonamides with heparin with hyperthermia or with intravenous injections of typhoid paratyphoid vaccine than with sulfonamides alone The percentage of cures by any of these methods is probably not significantly more than 5 5 per cent

The elevated leucocyte count returns to normal, as the temperature drops and other signs of infection disappear At the same time the hemoglobin increases and the rapid sedimentation rate gradually falls to normal However, the sedimentation time is an unsatisfactory guide to the effectiveness of treatment because in many cases it does not return to normal until several weeks after treatment has been discontinued and convalescence established

It has been observed repeatedly that petechiae and emboli to the viscera and the extremities may occur long after blood cultures are negative, and there are no evidences of active bacterial infection This is not remarkable in view of the observation of non infected emboli in the bacteria free cases described before the penicillin era While occasionally during the course of the treatment embolization associated with a transient elevation of the temperature is not followed by positive blood cultures in other instances embolization is a consequence of ineffective treatment and is accompanied by positive blood cultures

As in the cases recovering spontaneously, splenomegaly regresses, when a cure is effected by penicillin, splenomegaly usually disappears within a few weeks

Toxic Effects of Penicillin

Despite the administration of huge doses, up to 10 million units daily, toxic effects due to penicillin are rare and never serious Occasionally a generalized urticaria results, but it disappears despite continuation of penicillin therapy Occasionally the urticaria occurs after therapy has been completed

Causes of Failures in Penicillin Treatment

Most of the failures in treatment with penicillin have been due to extremely high resistance of the causative organism or to inadequate penicillin dosage The latter type of failure occurred chiefly in the early days of penicillin, when the drug was not available in adequate amounts or even more recently, before it was realized that doses of 200 000 units daily for 2 or 3 weeks sufficed for many cases but was inadequate for many others In at least some of the cases in which the causative organism is highly resistant, a cure nevertheless may be obtained with the massive doses now available

In some cases a cure was not effected despite a large total dosage of penicillin, because inadequate amounts were given at first, or treatment was interrupted prematurely During this period the disease progressed in such a manner as to preclude a cure even when eventually adequate doses were administered for long periods of time There is an element of chance in determining which cases may continue for long intervals without serious complications and which ones develop such complications early in the course of their disease It is certain that

delivered A full term child may be obtained also when the mother's infection does not respond to penicillin Even when the infant's blood gives a positive culture of the causative organism the bacteremia in the infant rapidly subsides If death of the prospective mother from bacterial endocarditis is imminent a Caesarian section is indicated provided the fetus is viable

Surgical Measures of Treatment

Ligation and Section of Ductus Arteriosus — Recovery from subacute bacterial endarteritis in a patient with patent ductus arteriosus following section of the ductus was first reported by Touroff and Vesell[13] It is probable that the cure is due to elimination of the impact of the blood on the wall of the pulmonary artery by way of the ductus In a subsequent report Touroff[14] documented 11 cases in which patients with a streptococcus viridans endarteritis complicating a patent ductus were subjected to ligation or section of the ductus Nine patients survived the operation 2 died of operative hemorrhage Of the 9 survivors 6 recovered By 1943 operation by various surgeons on a total of 33 such cases resulted successfully in 20 in surgical death in 5 and in persistence of the infection in 8 Since then other cases have been operated upon with cure

It is uncertain what part these surgical procedures will retain now that penicillin therapy promises an extremely high percentage of success When successful the surgical procedure cured not only the bacterial infection but also the anatomical defect Nevertheless if the causative organism is relatively sensitive to penicillin therapy should be started with this substance as in the usual cases of subacute bacterial endocarditis The indications for subsequent ligation or section of the patent ductus if the bacterial infection is cured will have to be reconsidered and revised in view of the therapeutic efficacy of penicillin Elimination of the patent ductus may be necessary if these patients prove especially susceptible to reinfection or if there is great danger of subsequent infection with less sensitive organisms Surgery may be indicated also in the presence of cardiac failure after bacteriological cure Finally ligation or section of the ductus still is indicated in cases of bacterial endarteritis due to organisms entirely resistant to penicillin and in cases with apparently sensitive organisms but in which there is no favorable clinical or bacteriologic response to adequate penicillin therapy

Resection of Arteriovenous Aneurysm — Similar problems are posed by the rare instances of arteriovenous aneurysm which becomes the site of a subacute bacterial angeitis Hamman and Rienhoff[22] described a case in which non hemolytic streptococci were implanted upon a previously existing arteriovenous aneurysm of the iliac artery and vein Resection of the aneurysm led to complete recovery the blood culture becoming negative within 2 hours and remaining so The absence of a cardiac murmur led them to conclude that the clinical picture was

only slightly better than that occurring spontaneously and disappointing at best Sulfonamide therapy must be relegated to a minor role in the treatment of sub acute bacterial endocarditis and then only for cases due to organism resistant to penicillin streptomycin or other bacteriostatic or bacteriocidal agent

General and Symptomatic Treatment

Rest in bed is mandatory at least as long as fever persists When penicillin is being administered by continuous venoclysis the patient necessarily is confined to bed, but within the limitations imposed by the intravenous setup motion of the body and especially of the feet and legs should be encouraged If the response to penicillin is favorable, and the drug is being given by intermittent intramuscular injection, bathroom privileges are permissible, when the patient becomes afebrile Further removal of restrictions of activity are dependent on the clinical course In the presence of heart failure confinement in bed or in a chair may be important even when fever has disappeared but activity may be resumed as tolerated when the infection is eradicated, and evidences of heart failure are controlled by more specific therapeutic measures

The patient's strength and well being should be conserved during the febrile period not only by rest in bed but also by a high caloric, bland diet supplemented by vitamins Unfortunately the patient's appetite usually is poor and he loses weight as long as the infection persists With a favorable response to penicillin the appetite returns promptly and the weight increases rapidly

The treatment of the anemia which usually is present, is of secondary im portance Transfusions usually are advisable when the hemoglobin falls below 60 per cent, but penicillin therapy should not be delayed in order to give trans fusions In extreme cases in which transfusions appear indicated at the outset penicillin should be given intramuscularly at the same time As a rule the hemoglobin rises progressively with a good clinical response to penicillin There fore in most cases the advisability of administering transfusions or iron can be decided at the termination of penicillin therapy If heart failure is present trans fusions should be given by very slow intravenous drip and preferably in 250 to 300 c c quantities The transfusion of packed red blood cells in glucose solution may be preferable in patients with diminished cardiac reserve

The treatment of heart failure embolism, embolic aneurysms and other com plications is the same as when they occur with other conditions Subarachnoid hemorrhages are not always fatal Lumbar puncture in some of these cases may be of definite value but the fluid should not be removed in too great a quantity or too rapidly

The management of the disease is not altered when it occurs during pregnancy With penicillin therapy the mother can be cured and a full term healthy child

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not due to subacute bacterial endocarditis This reasoning was not entirely correct, because the latter disease can occur without the development of a murmur However it is fortunate that the surgical procedure was performed It proved definitely what has always been believed that there exist cases in which the whole clinical picture is due to the local bacterial vascular disease

Two other cases of streptococcus viridans endarteritis of an acquired arteriovenous aneurysm were cured by excision of the infected aneurysm (Touroff Lande and Kroop [13], Lipton and Miller [16]) In the few previously reported cases of infection of a pre existing arteriovenous aneurysm (Bretscheider[9], Porter and Williams[60] Walz) an infection of the endocardium was present also

If as is likely penicillin therapy proves effective in these cases excision of the arteriovenous aneurysm would be indicated after bacterial cure only if there were serious circulatory disturbances It would also be indicated if the causative organism were resistant to penicillin or if a favorable therapeutic result could not be obtained for any other reason

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CHAPTER XI

THE CLINICAL ASPECTS OF CARDIAC ARRHYTHMIAS*

By SAMUEL A. LEVINE

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INTRODUCTION

The recognition of cardiac arrhythmias per se is of considerable importance for three distinct reasons. In the first place they may be either disturbing to the patient or make him unusually apprehensive of some serious cardiac disability. Secondly, the correct interpretation of a disturbance in the mechanism in the heart beat occasionally may be the

* The electrocardiography of these arrhythmias is discussed in the next chapter, chapter XI A, "Clinical Electrocardiography" by Francis F. Rosenbaum.

single clue to the diagnosis of an underlying disease which otherwise might be entirely overlooked. Finally, certain arrhythmias may be the sole cause of serious conditions threatening the health or even the life of the patient. In other words, apart from what else may be going on, the intelligent control of an arrhythmia may make the difference between recovery and continued disability, or occasionally between normal health and death.

The time long since has passed when a physician can be content to say that the heart is "slightly irregular" or that the beat is "more regular" without making an attempt to name the irregularity. One case may show a slight irregularity when it is a benign sinus arrhythmia, and another may appear no more irregular and be due to auricular fibrillation. It would be just as logical to say that a patient has a slight fever and then fail to ascertain whether the fever were due to typhoid fever, undulant fever or cerebrospinal fever. We should therefore try to recognize the various irregularities and call them by their proper names.

The exact diagnosis of irregularities of the heart is best obtained by electrocardiography. This subject has been taken up in the following chapter (Chapter XIA, Vol. II, of this system of medicine). The purpose of this discussion is to consider the simple bedside means of diagnosis and to analyze the clinical significance of the various arrhythmias and their treatment. It is not always possible and often not necessary to obtain electrocardiograms. Certainly it is more expensive and time consuming to take heart tracings than it is to use a stethoscope, and it will be seen readily that most of the diagnoses can be reached at the bedside with no more aid than any practicing physician carries with him in his every-day work. It must be admitted that some irregularities are so bizarre and difficult to decipher that we are forced to resort to electrocardiography for their correct diagnosis. As a corollary to this it is also true that those most familiar with electrocardiography will best be able to arrive at proper interpretations of auscultatory findings without heart tracings. *In other words, a knowledge of electrocardiography enables the* physician to get along all the better without it. However, there are numerous simple clinical observations easily elicited that will unravel many of these perplexing questions.

The Normal Heart Rhythm

Under normal circumstances the heart beat is fairly regular and the basal rate will vary in different individuals from about 60 to 90. Heart beats do not recur with absolute mathematical regularity, as there are

minor differences in the length of different heart cycles dependent on breathing and other nervous influences Patients differ in their normal basal rates just as they do in the blood pressure the metabolic rate the color of the hair and other bodily features In the normal heart two main heart sounds are audible over the precordium the first and second sounds (Fig 1) The first is mainly if not entirely due to the closure of

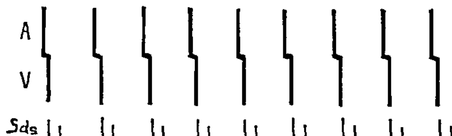


FIG 1 A represents auricular contractions V ventricular contractions the short diagonal line between A and V is the conduction time from auricle to ventricle this notation is used throughout all of the figures In Fig 1 Sd indicate first and second heart sounds

auriculoventricular valves mitral and tricuspid The second sound is due to the closure of the semilunar valves aortic and pulmonary The interval between the first and second sound is systole and that between the second and first is diastole Occasionally one can hear a faint third heart sound in mid diastole in normal individuals Ordinarily the contractions of the auricles produce no audible sounds The normal impulse starts at the sinoauricular node which lies at the juncture of the vena cava with the right auricle It then travels rapidly over both auricles causing them to contract simultaneously and continues to the ventricles through the junctional tissue This conduction pathway between auricles and ventricles lies in the upper part of the interventricular septum and consists of an auriculoventricular node Tawara node which continues into the so called bundle of His This then divides into two branches a right and left each going to the respective ventricle The impulse finally spreads throughout the ventricular musculature by means of an elaborate network called the Purkinje system enabling the ventricles to contract simultaneously There is a delay of the impulse in the junctional tissue so that the ventricle contracts somewhat less than 0 2 seconds after the auricles Normally this process repeats itself about 70 times a minute

single clue to the diagnosis of an underlying disease which otherwise might be entirely overlooked. Finally certain arrhythmias may be the sole cause of serious conditions threatening the health or even the life of the patient. In other words, apart from what else may be going on, the intelligent control of an arrhythmia may make the difference between recovery and continued disability or occasionally between normal health and death.

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tion (Fig 2) it may occur independently of breathing The changes in the length of the heart cycle are gradual and take place almost entirely at the expense of the length of the diastolic pause systole remaining essentially unchanged It has been called also respiratory or juvenile arrhythmia It is a normal disturbance very prominent and common in infants and children but also met with throughout life It is noted frequently after full digitalization It disappears when the heart rate becomes rapid from any cause such as fever emotion exercise or hyper



FIG 3 Note slow normal regular sequence of auricles and ventricles

thyroidism When the heart rate has been rapid for some cause the appearance of sinus arrhythmia suggests that recovery or convalescence is taking place and in that sense is a favorable sign When very marked it may be confused with arrhythmias having a more pathological significance Ordinarily it can be recognized easily by noting the gradual increase and decrease of the heart rate with respiration and particularly by observing that the heart becomes perfectly regular after a brief effort Sinus arrhythmia occurs for the most part in healthy hearts but also may be observed when the heart is diseased It is not an evidence of heart disease does not make the prognosis worse when heart disease is present and requires no treatment

NORMAL BRADYCARDIA

The rate of impulse formation may be slow and when it is below 50 a minute the condition may be called normal bradycardia Here the events occurring in the heart are normal except that the rate is slow (Fig 3) This is found in some perfectly healthy people especially in young tall individuals occasionally during convalescence from infections with jaundice and with inanition It probably indicates an increased vagal tone and is not an evidence of heart disease Its importance lies in the fact that it must not be confused with a slow heart due to heart

Although a regular beat within the normal range about 70 generally signifies a normal mechanism that by no means is true always It will be seen later that occasionally conditions such as auricular flutter, auricular fibrillation heart block and nodal rhythm may all have perfectly normal regular ventricular rates in the vicinity of 70 In many instances the underlying abnormal mechanism may be diagnosed or at least suspected by simple bedside means such as the effect of exercise or vagal stimulation though often it is impossible without graphic tracings

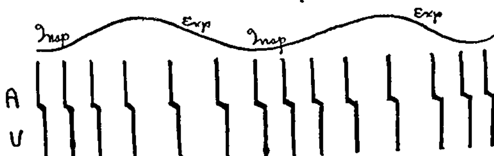


FIG 2 Note gradual slowing and acceleration of beat with phases of respiration

Disturbances in the rhythmic contractions of the heart beat must be analyzed mainly by careful auscultation of the heart Changes obviously result in the peripheral pulse but the character of such alterations cannot be analyzed accurately in most cases by a study of the pulse Similar hesitation or intermittence of the radial pulse may be due to a variety of mechanism The particular one involved in any given instance generally will become clear only after the heart sounds themselves are studied critically It cannot be overemphasized that auscultation is of primary importance in this respect

SINUS ARRHYTHMIA

The rate and rhythm of the normal heart beat is controlled by a double nervous mechanism the vagus which tends to slow the heart and the sympathetic which tends to accelerate it Even under normal conditions the adjustment is not mathematically exact so that very slight differences in the length of consecutive cycles occur especially with different phases of respiration When these rhythmic alterations are more pronounced the condition is called sinus arrhythmia Although the acceleration and retardation of the rate generally is phasic with respira

Sinus Pause

Amongst the rare cardiac irregularities there is one in which the heart beat stops for a brief interval In this condition there is complete asys tole for a varying length of time because the production of an impulse is delayed (Fig 5) It is called sinus pause and needs to be distinguished



Fig 5 Note sudden slowing of both auricles and ventricles The length of the pauses is not a multiple of the normal heart cycle

from heart block In the latter conditions an impulse is formed but blocked somewhere in its passage while in the former the impulse is not even made When sinus pauses occur the asystole that is observed varies in duration and the subsequent pace of the beat is disturbed In heart block the length of the pause will be approximately a definite multiple of the normal heart beat with the subsequent beats remaining undisturbed

Sinus pauses result from stimulation of the vagus nerve Sensitivity of the carotid sinus is one of the mechanisms responsible There are numerous other reflexes that stimulate the vagi and thereby produce un usual slowing or more outspoken pauses in the heart beat The severity of the symptoms will depend on the degree of the slowing When it is marked actual syncope may result and thereby resemble Adams Stokes disease or epilepsy It is important to realize that sinus pauses occur for the most part in patients who have no heart disease the attacks often being precipitated by prolonged standing a sudden twist of the head an overheated or overcrowded room the sight of blood the prick of a hypodermic needle or other sudden emotional upsets On ausculta tation one hears a marked slowing of the heart or a sudden pause gen erally accompanied by a fall in blood pressure

In most cases treatment is unnecessary and attacks are very rare Nothing disastrous is likely to result because if the asystole were to be very long the ventricles are apt to escape and initiate contractions from

block This is particularly so when the rate of normal bradycardia is 40 or less as occasionally occurs for then one readily might misinterpret the condition as complete or 2 to 1 heart block signifying serious heart disease when as a matter of fact the heart may be entirely normal

On auscultation one merely hears regular slow normal heart sound The rate will rise gradually on effort or as a result of drugs such as atropine adrenalin or amyl nitrite and gradually return to its former rate The clinical methods of distinguishing it from heart block will be taken up later Treatment is not necessary for normal bradycardia but should be directed at the underlying condition

Normal or Sinus Tachycardia

The heart rate may be rapid and perfectly regular with the beats following a normal course through the heart When the rate is over 120 arbitrarily it can be called normal or sinus tachycardia (Fig 4)

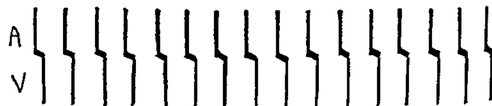


Fig 4 Note that although action is rapid and regular A–V sequence is normal

This is the natural response to effort emotion fever anemia shock hyperthyroidism and many other states It is obvious that sinus tachycardia may occur with heart disease but also is seen frequently in many non cardiac conditions When the rate is 130 to 150 or more it must be distinguished from other abnormal mechanisms in which the heart is rapid and regular This differentiation at times is very important and will be taken up in later discussions for whereas the abnormal tachycardias often are amenable to specific methods of therapy there is no treatment for normal tachycardia attention being directed at the underlying cause i e iodine for hyperthyroidism transfusion for shock or hemorrhage etc One important point to bear in mind is that the rapid rate of normal tachycardia is reached gradually over minutes hours or days while in the abnormal tachycardias the transitions are abrupt in seconds

tricular extrasystoles (Fig 8) depending on the focus of origin On auscultation after a varying number of regular normal cycles one hears a quick beat followed by a pause with the resumption of the normal sequence The premature beat may be faint or clicking in quality and it may or may not produce a peripheral pulse For that reason it may not be palpable in the radial artery It therefore can be confused with the dropped beat that occurs in partial heart block It must be evident however that in heart block there not only is a pause in the pulse but no beat is audible over the precordium as the ventricles do not contract whereas when extrasystoles occur during the pause that takes place in

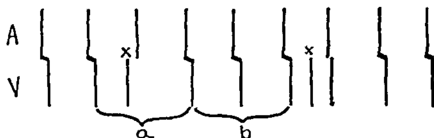


FIG 8 The premature beat arises in the ventricle (X) and the pause is completely compensatory so that a = b Note that the auricular beat occurring at the time of the extrasystole is not followed by a ventricular contraction because the ventricle *still is refractory At one point two consecutive extrasystoles occur*

the pulse an extra premature contraction can be heard over the heart Occasionally difficulties in diagnosis may arise because when extrasys toles occur very early in diastole the amount of ventricular filling may be so slight and the intraventricular pressure of that particular beat may be so low that the aortic valves are not opened and only one faint heart sound instead of two results This faint single sound may therefore resemble the distant auricular sound that occurs in heart block Finally there are rare occasions when extrasystoles take place and no audible sounds can be made out Electrocardiograms are neces sary for diagnosis under these circumstances

Extrasystoles may be very infrequent so that the physician does not detect them during his examination or they may be constantly present occurring every several beats When they occur every second beat the condition is called bigeminy (Fig 9) every third beat trigeminy etc At times there may be runs of two or more extrasystoles in quick suc

a pacemaker of their own When attacks are frequent however preparations like 25 mgm (3/8 grains) of ephedrine or ten drops of tincture of belladonna three times daily may be effective Occasionally a cervical gland or an enlarged thyroid may be the cause of such attacks and will need to be removed Very rarely resection of the nerve plexus around a sensitive carotid sinus is necessary

Extrasystoles Premature or Ectopic Beats

The normal regular beat may be interrupted by impulses arising prematurely in any part of the heart These are called extrasystoles or premature or ectopic contractions These may be divided into three main types auricular (Fig 6) nodal or junctional (Fig 7) and ven

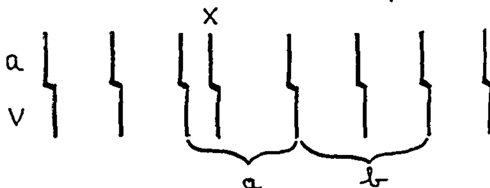


Fig 6 The premature beat arises in the auricle (X) and the pause is not completely compensatory so that interval a is less than b

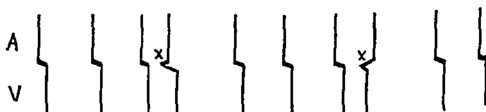


Fig 7 The premature beats (X) start at the A–V node and the impulse goes upward to auricles and downward to ventricles In the first one the auricles and in the second the ventricles contract first

tricular extrasystoles (Fig 8) depending on the focus of origin On auscultation after a varying number of regular normal cycles one hears a quick beat followed by a pause with the resumption of the normal sequence The premature beat may be faint or clicking in quality and it may or may not produce a peripheral pulse For that reason it may *not be palpable in the radial artery* It therefore can be confused with the dropped beat that occurs in partial heart block It must be evident however that in heart block there not only is a pause in the pulse but no beat is audible over the precordium as the ventricles do not contract whereas when extrasystoles occur during the pause that takes place in

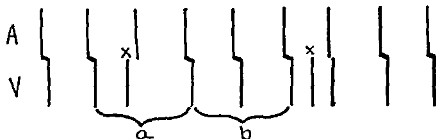


FIG 8 The premature beat arises in the ventricle (X) and the pause is completely compensatory so that a = b Note that the auricular beat occurring at the time of the extrasystole is not followed by a ventricular contraction because the ventricle still is refractory At one point two consecutive extrasystoles occur

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cession following a normal beat (Fig 8) Occasionally the heart rate is sufficiently slow or the ventricular extrasystole comes so early that the sequential auricular impulse finds the ventricle out of its refractory state

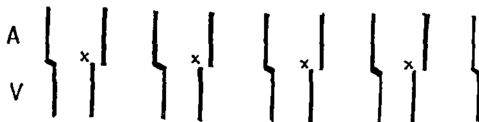


FIG 9 Every second beat (X) is a premature ventricular beat the auricles remaining undisturbed

In this case the extrasystole is interpolated between the two normal beats without any pause with the result that three consecutively quick beats are heard (Fig 10)



FIG 10 Ventricular beat (X) occurs between two normal beats Note that the auricular beat following X no longer finds the ventricles refractory

Symptoms — Extrasystoles may produce no symptoms and they are apt to be detected first on routine examination In many instances however they produce uncomfortable sensations and often considerable apprehension It will be found generally that patients with nervous temperaments and particularly thin chested individuals will be disturbed particularly by these beats It seems that the more obese or thick chested individuals are less apt to sense vibrations made by the heart The symptoms produced by extrasystoles are described in a great variety of ways and yet there appears to be a similarity in expressions amongst

different cases The following terms are used often a skip of the beat a sudden flop or sinking sensation a wave comes over me the heart stops for a moment a sudden throb or choking sensation in the throat a feeling like the fluttering of a bird or the sudden splash of a fish in water the heart suddenly turns over etc. Some of these sensations are produced by the premature beat some by the pause that occurs and others by the forceful beat that follows the compensatory pause The patient s description often helps to identify the condition when the physician has not detected it during his examination

Extrasystoles are very common both with and without organic heart disease They must not be regarded therefore as evidence of heart disease They have been known to be present in otherwise healthy individuals for a great many years without producing any impairment of health For the most part they appear when the heart is slow or the patient is quiet For this reason they are particularly troublesome at rest while lying down and trying to fall asleep They are prone to disappear on exercise or when the patient is busy and his mind occupied In a small number of cases they are brought on only by effort

Causes — In most cases no specific cause can be found for their occurrence In very rare instances they result from excessive use of tobacco or of coffee Even when coffee and tobacco are used in excess generally they will be found to bear no relation to the development or disappearance of the extrasystoles The one drug commonly used that produces them is digitalis In fact the appearance of extrasystoles previously not present during the administration of digitalis is the first evidence of a toxic action of this drug When this effect becomes more marked ventricular extrasystoles occur after each normal beat producing a bigeminy or what is termed digitalis coupling Digitalis should be omitted temporarily when this occurs

In most instances in which organic heart disease is absent no specific cause will be found for extrasystoles and then they are regarded as functional or neurogenic in origin Emotional factors play an important role In recent years animal experimentation has thrown considerable light on this problem for anatomical pathways have been traced from the hypothalamic region to the heart that control extrasystoles Inasmuch as the hypothalamus is regarded as an important center of the emotions there now exists a clearer background for the production of so-called functional or benign extrasystoles

When extrasystoles occur with organic heart disease they may have some special significance During acute coronary thrombosis they may serve as a slight warning that arrhythmias of greater importance may

develop For this reason some authorities suggest giving quinidine under these circumstances with the hope of preventing the development of ventricular fibrillation and sudden death In following patients with mitral stenosis having a regular rhythm the appearance of auricular extrasystoles may serve as a warning that auricular fibrillation may develop soon There is one other condition in which the detection of extrasystoles and their correct interpretation may be helpful If patients have attacks of rapid heart action and it is difficult or impossible to observe the attacks because of their brevity or infrequency the finding of auricular extrasystoles would suggest strongly that the attacks are paroxysms of auricular tachycardia or fibrillation and the finding of ventricular extrasystoles would point to paroxysms of ventricular tachycardia or even on extremely rare occasions transient ventricular fibrillation Occasionally such inferential observations are the only means available for making these important decisions

Diagnosis — The distinction between auricular and ventricular extrasystoles is established easily by electrocardiograms but often can be made out at the bedside In general the auricular extrasystole sounds like a normal cycle only occurring prematurely The ventricular type on the other hand has a peculiar clicking or abnormal quality The latter also is followed by a completely compensatory pause except for the interpolated ventricular extrasystole when three quick beats are heard while with the former the pause generally is shorter (Figs 6 and 8) The difference in the character of the first heart sound with the two types of extrasystoles is the result of the following mechanism In auricular extrasystoles the ventricular contraction follows the auricular in normal sequence although prematurely and the mitral and tricuspid valve leaflets are caught in about the normal position at the time of ventricular systoles When a ventricular extrasystole occurs the auricles have not contracted as yet have not pushed down these valvular leaflets with the result that ventricular systole finds them in a different position Inasmuch as the first sound is made almost if not entirely by the valvular snap it will differ in these two types of beats

Another observation that may aid in distinguishing ventricular from auricular extrasystoles is that with the former one often can see a sudden large wave in the jugular pulse This takes place because at that moment the auricles contract while the ventricles are in systole and the auriculo ventricular valves are closed Blood thereby is forced backwards from the right auricle up the superior vena cava to the jugular vein

Nodal beats are comparatively rare and their recognition will de

pend on electrocardiograms Their presence occasionally may be suspected if their origin is shifting from time to time (Fig 7) because in this way the character of the first heart sound may vary considerably as a result of the same mechanism just discussed for the relation between auricular and ventricular systoles will be changing

Treatment —The treatment of extrasystoles will vary considerably under different circumstances When it is decided that there is no organic disease it will depend on whether they are frequent or troublesome Often they are found accidentally the patient being entirely unaware of their presence Under these circumstances no therapy is indicated It might be wise to explain to the patient that an occasional irregularity is present and that it has no practical significance does not mean heart disease and should not interfere with normal activities If this is not done some other physician might misinterpret its meaning and arouse unnecessary fears in the patient s mind This simple explanation of its benignity will suffice for extrasystoles often come and disappear for no good reason

When extrasystoles are annoying and persistent and not due to some specific cause that can be eliminated quinidine sulfate often proves beneficial The dose necessary may vary considerably Using an 0 2 gram (3 grain) tablet it will be found that from one half tablet to two tablets three times a day is often helpful Some authorities believe that the addition of 0 6 mgm ($\frac{1}{100}$ grain) of strychnine sulfate to each dose of quinidine increases its effectiveness In some cases quinidine may be given only one half to one hour before the irregularity is most apt to occur This method is particularly useful when palpitation comes at night or bed time The dose of the drug should be continued long enough to ascertain whether it is effective and should be discontinued if it proves useless It should be discontinued also after an appropriate length of time if the irregularity is controlled to see if the drug is needed any longer

Although many other drugs have been used in the treatment of extrasystoles the results have not been very impressive Occasionally it appears that when the irregularity has not been the result of digitalis, comparatively small doses of the drug such as 0 1 gram (1½ grains) twice daily may be helpful Atropine in the form of 10 drops of tincture of belladonna three times daily may tend also to inhibit extrasystoles by diminishing vagal tone or by increasing the heart rate Finally on rare occasions potassium salts in the form of 1 gram (15 grains) of potassium chloride or phosphate three to four times daily have made premature beats disappear when all other measures failed

When extrasystoles accompany other important diseases the underlying conditions deserve the same treatment that would be given if the heart is regular. This applies particularly to organic heart disease. If digitalis is required and has not been responsible for the development of the irregularity it should be given in the usual way, only somewhat greater caution should be exercised in watching for toxic evidences.

PAROXYSMAL AURICULAR TACHYCARDIA

All physicians have seen instances in which the heart suddenly becomes very rapid and regular and after a variable length of time just as abruptly returns to a normal rate. It has been thought under these

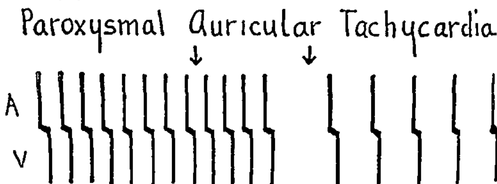


FIG. 11. Note rapid perfectly regular sequence of auricular and ventricular beat followed by a sudden cessation of the attack and the return to a normal slow beat as a result of carotid pressure indicated by arrow.

circumstances that some ectopic focus in the auricles takes over the pace of the heart sending out regular rapid beats that travel through the auricles in an abnormal route then down the junctional tissue to the ventricles normally. There is reason to suspect that in some of these cases a circus movement is taking place in the auricles somewhat similar to what occurs in auricular flutter but that the pathway may be different. This condition generally is called *paroxysmal auricular tachycardia* (Fig. 11).

If the condition is observed during an attack one hears a perfectly regular rapid heart at a rate of 150 to 250. If one is fortunate enough to auscult the heart at the time of the onset or offset the change from slow to rapid rates or vice versa will be heard to take place within one heart cycle in the great majority of cases. Furthermore while the heart is rapid the sounds are all alike in quality and intensity.

This type of paroxysmal tachycardia is quite common and occurs

both with and without accompanying organic heart disease In fact it is much more common as a purely functional disturbance in otherwise healthy individuals The history of attacks is often quite characteristic The patient complains that *without apparent cause or as a result of a sudden disturbing thought or motion of the body such as stooping to tie a shoe or turning the head the heart suddenly begins to palpitate* With this there *may be momentary faintness or rarely actual* syncope general nervousness and apprehension In most cases there is no dyspnea or pain In some however typical anginal pain may result and in others congestive heart failure may develop

The severity of the symptoms that follow an attack will depend on these factors the duration of the attack the heart rate during the attack and the condition of the heart before the attack It is obvious that a normal heart might tolerate a very rapid rate without embarrassment much longer than one with mitral stenosis When organic heart disease is already present pulmonary and hepatic congestion may develop in a few hours with a rate of 180 On the other hand a normal heart may show no evidence of failure with a rate of 200 even after a day or more

When the attack *is prolonged and severe certain important findings may result Occasionally a slight fever of 100 to 101° F and an appreciable leucocytosis of 15 000 or more occur* There also may be a sharp drop in the blood pressure and some rales at the bases of the lungs All these features together with appearance of shock that may be present especially if in addition there is pain in the chest resemble very closely the picture of acute coronary thrombosis with which it easily can be confused The distinction is important because in the one case when recovery takes place the heart is normal while in the other it is not In this connection it is well to recall that whereas cardiac irregularities are very common with acute coronary thrombosis paroxysmal auricular tachycardia is extremely rare during such an attack Further confusion may arise because coronary thrombosis or thromboses of other vessels *actually may result from the prolonged rapid heart action with the accompanying fall in blood pressure and occasionally emboli complicate* attacks

Attacks of tachycardia vary considerably in their frequency and duration They may last only several seconds or minutes or continue for hours or days uninterruptedly A patient may have one attack under peculiar circumstances and never have any more In most cases however paroxysms tend to recur In extreme cases only a few hours may intervene between attacks on the one hand and as long as years on the

other hand There is no method of predicting these recurrences except through prolonged observation Furthermore, the rate of the heart during the attack is apt to be characteristic for each particular case one tending to have a rate of about 170 in each attack while another always will have a rate of about 220

Symptoms — Generally this condition is harmless though frequently annoying Most patients are perfectly well shortly after the attack is over and in fact some can carry on their customary duties even while the attack is on Occasionally alarming symptoms result and very rarely fatalities have occurred When it develops during the course of a general anesthesia or a surgical operation disastrous results may ensue unless the attack is stopped promptly I have seen an instance in which the patient became pulseless and respiration ceased with instant recovery as the paroxysm was controlled by appropriate treatment Finally there are rare occasions when the peripheral circulation is so sluggish that thromboses of vessels occur The blood pressure may fall to such an extent that the pulse pressure may not be any more than 4 to 6 mm of Hg When such a condition persists for hours and days cerebral accidents such as aphasia and hemiplegia may result or gangrene of a limb may occur I have seen such complications in a case in which the heart beat continued incessantly for days at a rate of 250 It was unfortunate that these complications did occur in this case as they were preventable When I first saw this patient in an attack it was controlled readily by vagal stimulation and he was taught how to do it himself From then on he never suffered any further disabilities though he had occasional short paroxysms during the subsequent years He had however lost an arm from one of his earlier attacks

Diagnosis — The diagnosis of paroxysmal auricular tachycardia generally is not difficult especially if one can observe the patient in the attack The history itself may be quite characteristic but in all forms of paroxysmal rapid heart action the attack itself must be witnessed to be absolutely certain of the type of paroxysm Otherwise one will be in doubt whether the heart was temporarily rapid and irregular or rapid and regular or whether there was merely a slight acceleration of a normal beat In fact the condition may be confused with various types of ' indigestion as the patient often is convinced that all his trouble is due to the stomach or to gas This conviction is fortified by the observation made by many that the attacks end when vomiting or belching of gas takes place In these cases the physician should make every effort to study at least one attack Because they come suddenly and at odd times he should be ready to leave his work or his bed to identify

the type of disturbance Only in that way will he be able to outline intelligent therapy

During the attack the patient generally will be found in no great distress It is striking how little disturbed he may be with such a rapid heart The heart will be perfectly regular and rapid with a rate between 150 and 250 often around 190 and the sounds of each cycle all appear *to be the same The absolute regularity is an important characteristic* and for this reason the rate should be counted accurately for 60 seconds This can be done without error if care is taken and the rhythm is regular Tapping the foot or the finger during auscultation may help considerably in obtaining accurate counts *After this is accomplished* attempts to change the rate should be made such as having the patient exercise a bit if he can or bend up and down in bed or hold his breath The heart rate then should be counted again *If it is paroxysmal tachycardia* it will be found unchanged The error should not be greater than two beats which can be accounted for by the timing of the first and last beat as the second hand of the watch makes its circuit of one minute *If there is an appreciable difference in the two counts five beats or more* the condition is likely to be a normal sinus tachycardia and not a paroxysm Occasionally as during pneumonia or thyrotoxicosis this differentiation is important If the first count was 163 and the second was 170 the condition is much more likely to be a normal tachycardia due to some underlying disease while if both counts were 163 it would suggest an abnormal tachycardia as the latter state is uninfluenced by the *procedures mentioned above*

The second method of establishing a diagnosis is the use of vagal stimulation This can be carried out in a variety of ways the simplest one of which is by irritation or massage of the carotid sinus At the bifurcation of the common carotid artery into the internal and external carotids there is a bulge or prominence of the vessel and surrounding the vessel at this point there is a nerve plexus which reflexly stimulates the vagus nerve *When this region is manipulated* a normal heart rate should slow gradually and then return to the previous level In paroxysmal auricular tachycardia temporary massage of the carotid sinus often stops the attack instantly (Fig 11) There may *follow a short temporary* asystole occasionally interrupted with a premature beat and then an abrupt resumption of the normal heart beat There is no other condition in which a very rapid heart rate can be stopped promptly by this method If the attack *ends in this fashion* therefore it establishes the diagnosis of paroxysmal auricular tachycardia There are frequent instances in which no effect will be produced by vagal stimulation In

this case the diagnosis still may remain in doubt The important point to bear in mind is that carotid sinus stimulation will either stop the attack completely or will have no effect whatever If the rate is about 160 to 170 and there is a gradual smooth slight slowing with a gradual return of the rapid rate as stimulation is released the condition is a normal sinus tachycardia However when there is a temporary slowing more or less marked with an irregular jerky return of the rapid rate the tachycardia is likely to be due to auricular flutter (Fig 12)

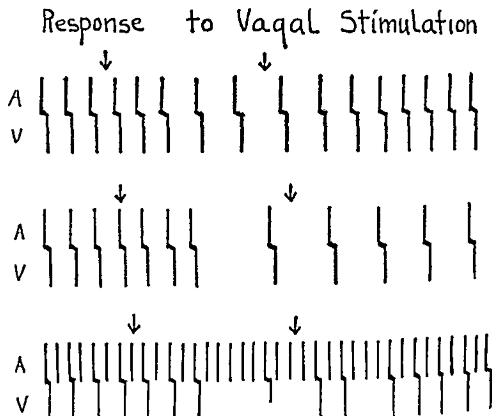


FIG 12 Arrows indicate duration of carotid sinus stimulation Upper graph shows smooth gradual slowing and return to original normal rapid rate in *sinus tachycardia* Second tracing shows abrupt cessation of attack in *paroxysmal auricular tachycardia* Lowest graph shows temporary slowing with jerky irregular return of rapid rate in *auricular flutter* All three started with regular ventricular rate of 160

The above discussion pertains to the common type of paroxysmal tachycardia There is a rarer form not so clearly understood in which there may be an accompanying heart block a condition that never is found in ordinary paroxysmal tachycardia In this regard it resemble

auricular flutter but the electrocardiograms fail to show the characteristic auricular waves of flutter

Treatment — There are two aspects to the treatment of paroxysmal auricular tachycardia the treatment of the attack itself and the prevention of recurrences There are various methods in use to stop the attack some of which patients themselves learn how to employ The simplest is to take a deep breath and to hold it for as long as possible This often is very effective Other procedures are inducing retching or vomiting by having the patient put his finger down his throat The most useful is carotid sinus stimulation mentioned above It is best to manipulate one side at a time and not both simultaneously After finding the proper part of the carotid artery firm massage is carried out with the fingers of one hand pressing backwards against the spine First one side then the other is tried When this fails ocular pressure may be tried For this purpose ocular pressure must be applied rather vigorously This procedure is likely to be painful but occasionally it will restore the normal rhythm when other methods are ineffective It is particularly useful when attacks occur under anesthesia for then pain will not be felt

A great variety of other techniques in one case or another has appeared to be valuable Swallowing bits of ice pressing firmly on the abdomen lifting the foot of the bed while keeping the head low and even a simple dose of 0 3 mgm to 0 6 mgm (1/200 to 1/100 grain) of nitroglycerine sublingually all have been successful Often the physician gives a hypodermic of morphia or a simple sedative returns in an hour or two and finds the heart normal When attacks stop in a few seconds or minutes after the employment of any of the above procedures it is likely that the treatment was effective but when the attack ends an hour or more later one may not be sure of the relationship of cause and effect

When attacks persist for hours despite the use of the simple procedures just enumerated various drugs may be employed One to four teaspoonsful of syrup of ipecac by mouth and repeated in an hour or so often is very effective This produces fairly severe vomiting and vagal stimulation but no lasting untoward effects When it works it generally brings the attack to an end in about 15 minutes Apomorphine 6 mgm (1/10 grain) subcutaneously has a similar but less reliable action Quinidine sulfate 0 13 to 0 3 gram (grains 2 to 5) intravenously can be very effective and stop attacks within several seconds but it is dangerous and should not be employed except as a last resort Digitalis on the other hand in doses of 0 5 to 0 6 grams (7½ to 10 grains) intravenously

for adults who have had no other digitalis recently is a safe procedure but one that only occasionally will be found useful Finally acetyl beta methylcholine (mecholin) 0 020 grams (1/3 grain) subcutaneously is one of the most reliable vagal stimulants for this purpose In many cases the attack will be controlled within 5 to 15 minutes but there is a slight risk in its use This risk can be diminished if not avoided by always having 1 to 2 mgm (1/60 to 1/30 grain) of atropine sulfate ready for immediate use should severe vagal symptoms develop and by keeping a tourniquet ready to compress the limb above the point of injection, if necessary to prevent further absorption of the drug

It can be seen readily that there are many methods of treatment available If one fails another may work It is extremely rare that attacks cannot be controlled Frequently just as the physician begins to wonder what he should do next the attack ends spontaneously If it should last and the condition becomes critical the use of some of the above drugs intravenously or subcutaneously is warranted realizing that there is some risk

The second aspect of the *treatment* is *more difficult* Generally it is easy to stop the attack but difficult to prevent recurrences When they come at rare intervals it is best to advise no constant medication being content to meet each spell as it arises Not knowing when such an attack may come it would be hardly worthwhile to institute daily administration of some medication in the hope of preventing an attack that may not develop for a year or more When they are frequent the constant administration of digitalis or quinidine may prevent them effectively In my experience digitalis has been more successful *The drug needs to be given in full therapeutic doses just* below the point of producing nausea and must be continued indefinitely Giving the drug one month and then omitting it does not prevent attacks from occurring in later months After an adequate trial of digitalization if attacks recur with about the same frequency or intensity the drug should be omitted entirely Then quinidine may be tried in doses of 0 2 to 0 3 grams (3 to 5 grains) three times daily A given dosage should be continued long enough to judge whether the frequency of the spells is diminished and if not it should be omitted or increased Generally if 0 3 grams (5 grains) three times daily is ineffective it is best to discontinue quinidine although occasionally larger doses may be effective Some cases are refractory to both digitalis and quinidine and then we fall back on the problem of treating each attack as it comes Whether other medication such as potassium salts or sedatives are effective is open to question

Auricular Flutter

One of the comparatively rare arrhythmias due to disturbances in the auricles is *auricular flutter* It is about one tenth as common as auricular fibrillation *This condition is due to a circus movement in which an impulse runs around the auricle perfectly regularly and rapidly* at a rate of about 250 to 350 The auricles contract with each one of these impulses but the junctional tissue cannot conduct such a large number The result is that there is some degree of heart block in almost all cases of flutter Only very rarely will all beats succeed in



Fig 13 The auricles are beating perfectly regularly rate 320 the ventricles perfectly regularly rate 160 Every other auricular impulse blocked

reaching the ventricles It must be appreciated always that the auricular activity is inferred generally from what the ventricles do as the contractions of the former are not heard On auscultation we hear ventricular not auricular systole In auricular flutter therefore the auricular rate may be 320 but the audible heart rate over the precordium and the pulse rate is likely to be 160 In fact when flutter has not been treated most cases will show a 2 to 1 block so that the auricular rate will be twice the heart rate as counted at the apex *It is also evident that if the auricular rate is perfectly regular and every other beat is blocked* the ventricular rate will also be perfectly regular (Fig 13)

Diagnosis —At this point we must make clear that a heart may be rapid regular and at a rate of about 160 under three different circumstances If the mechanism is normal but merely rapid it is ***normal or sinus tachycardia*** Secondly it may be ***paroxysmal auricular tachycardia*** discussed in the preceding section with the same number of auricular and ventricular contractions Finally it may be ***auricular flutter*** with an auricular rate of 320 In all three instances the heart will sound alike *Generally it is not difficult to distinguish the three at the bedside* The

characteristic response to carotid sinus pressure in each of the first two of these conditions has been discussed already (Fig 12) In most instances of auricular flutter there will be a temporary slowing of ventricles during vagal stimulation with a jerky return to the previous rapid rate If the tachycardia is brought to an abrupt end it must be paroxysmal tachycardia as no other condition responds in this way If there is a slight gradual slowing with a smooth return of the rapid rate it is normal tachycardia If no effect whatever is produced by carotid sinus stimulation, no conclusion can be drawn In auricular flutter the rapid auricular rate remains unchanged while the ventricles temporarily slow The only effect is a vagal inhibition produced at the auriculoventricular node or the bundle of His so that the degree of block is increased for a few seconds

Because of the great frequency of an accompanying 2 to 1 block in untreated cases of flutter the majority when first seen will have a regular heart rate between definite limits Inasmuch as the auricular rate is likely to be between 250 and 350 the ventricular rate will have to be between 125 and 175 On extremely rare occasions the auricular rate may be 360 to 400 in which case the audible heart rate will be between 180 and 200 I have seen such rare examples during pneumonia and thyrotoxicosis It follows from the above considerations that when the rhythm is regular at a rate in the vicinity of 204 to 222 the condition cannot very well be due to flutter but rather to paroxysmal tachycardia, for the auricular rate necessarily would be 408 to 444 which is too rapid or 204 to 222 which is too slow In this way by simple calculations of the expected auricular rates important diagnostic inferences can be made

After a case of auricular flutter has been started on therapy the situation changes and different criteria for diagnosis must be used Let us assume that the heart rate originally was 160 with auricular rate 320 After a certain amount of digitalis is given the ventricular rate will slow although the auricular rate remains unchanged The degree of block increases the ventricular rate slows to 120 and now is irregular There is now a varying degree of block so that every second third or fourth auricular impulse reaches the ventricles At this point the heart may sound very irregular and resemble auricular fibrillation If the possibility of flutter is kept in mind a clinical diagnosis may be made by having the patient exercise The heart is likely to return to the original regular rate of 160 for a brief time an effect that is never produced by effort if auricular fibrillation is present In some cases however electrocardiograms will be necessary to establish the correct diagnosis

On further digitalization more slowing of the heart will occur so that the above patient in a few days may develop a regular heart rate of 80 Now every fourth beat reaches the ventricles while the auricles still are in a state of flutter with a rate of 320 (Fig 14) If such patients

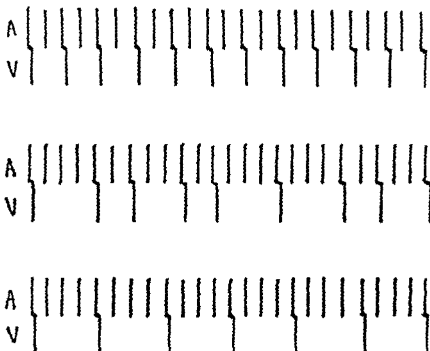


Fig 14 Upper graph before digitalis ventricular rate regular 160 Middle graph after partial digitalization ventricular rate irregular about 110 Lower graph full digitalization ventricular rate regular 80 Auricular rate 320 throughout

are seen first in this condition they are apt to be regarded as having a normal rhythm It would be difficult to suspect that the cardiac mechanism were abnormal if one heard a perfectly regular beat of 80 Here again one could uncover the true condition by means of a simple exercise test If such a patient were to hop 10 to 20 times the heart rate would jump suddenly to 160 and then in a minute or two become irregular but slower finally returning to the previous rate of 80 The fact

that the rate exactly doubled is important for it then is 160 or one half the auricular rate of 320. If it reached a regular rate of 118 or 137 it could not be flutter because there are no such simple fractions of the underlying auricular rate.

The above arithmetical considerations have more than theoretical interest. There have been times when it was possible to diagnose auricular flutter from the appearance of a hospital bedside chart. In one case it was noted that during the previous week the nurses' pulse chart of this particular patient showed many rates in the vicinity of 70 and without cause or change in the temperature many other counts around 135 to 140. From these observations alone it was suspected that auricular flutter was present, that the auricular rate was 280 and that when the nurse found the pulse 70 there was 4 to 1 block and when she counted it 135 to 140 there was 2 to 1 block. This very situation was found to exist when electrocardiograms were taken.

Auricular flutter generally is associated with organic heart disease either valvular or myocardial. It may be present also with thyrotoxicosis. In a small number of instances it is a purely functional disturbance without any other evidence of organic heart disease or other detectable disease. It may recur as a transient phenomenon just as paroxysmal auricular tachycardia, although in most cases it tends to continue for weeks, months or even years unless treated medicinally. Because of its tendency to persist and because of the ease with which the heart rate can accelerate it is a real handicap. In cases of auricular flutter receiving no treatment in fact there is always the possible danger of the ventricles suddenly responding to every auricular beat. If this happens the heart rate would jump suddenly to 250 to 350. With such an extremely rapid rate collapse or syncope readily might result. For this and other reasons it is generally wise to treat flutter with the hope of restoring a normal mechanism.

Treatment. — The treatment of auricular flutter is carried out best in a hospital where electrocardiograms can be taken whenever necessary, as there are times when it is difficult to determine the exact state of the heart beat without graphic methods. First digitalis is given in doses of 0.1 gram (1½ grains) three or four times a day. In a few days the heart rate will decrease. The original rapid regular beat will slow and become irregular. At this time it may sound like auricular fibrillation. Although with careful bedside study as discussed above the true situation may be recognized at times, electrocardiograms will be needed. Then in a day or so the heart rate may be normal and regular. At this point also the situation may be deceiving. The slow regular beat actually may be due

to a reversion to a normal rhythm or it may be a regular 4 to 1 block with the auricles still in a state of rapid flutter

In about one third of the cases after several days of digitalis therapy when about 15 doses of digitalis have been given auricular flutter changes over to auricular fibrillation and if at this point the drug is omitted a normal rhythm is resumed in a day or two. There are therefore three possible results following digitalis. The flutter may continue with a slower ventricular rate it may have changed to auricular fibrillation and either remain so or revert to the original flutter and finally a normal rhythm may have been restored. If the last result is obtained the main purpose of therapy has been accomplished. If auricular fibrillation develops the change has been worth while because this is more stable and the ventricular rate can be controlled more readily by constant digitalization. If flutter persists the slowing of the ventricular rate at least has improved the circulation

If digitalis fails to alter the state of flutter it is generally advisable to use quinidine. While the patient is fully digitalized and the ventricular rate is slow a daily maintenance dose of 0 1 gram (1½ grains) of digitalis is continued and increasing doses of quinidine are given. There are various methods of administering quinidine but the following is one that I have employed a great deal. Starting with a dose of 0 2 gram (3 grains) orally increasing amounts are given at 10 A M 2 P M and 6 P M. The dose is increased 0 1 gm (1½ grains) each time while careful observations are made of the effect of the previous dose. In this way 0 2 gram (3 grains) 0 3 gram (5 grains) 0 4 gram (6 grains) 0 5 gram (7½ grains) etc are given. Occasionally if circumstances require it and greater haste is necessary the amounts are increased more rapidly. During the quinidine administration two changes will be observed. The auricular rate of the flutter always will decrease and ventricular rate generally will increase. In the great majority of cases when an adequate amount of quinidine has been given the circus movement in the auricle which is responsible for the flutter will be broken and a normal rhythm will result. The gradual slowing of the auricular rate which can be determined accurately only by electrocardiograms is a reliable guide and shows that quinidine is having an effect and that more of the drug needs to be given. The amount necessary to accomplish this varies a good deal. Often it is obtained when a single dose of 0 5 gram to 0 7 gram (7½ grains to 10½ grains) is reached but occasionally as much as 1 5 grams (22 grains) has been necessary

When the heart has become regular it is customary to continue a maintenance dose of 0 2 to 0 3 grams (3 to 5 grains) of quinidine three

times a day for a few weeks This may be decreased gradually and finally omitted entirely Whether continued quinidine therapy is at all necessary and for how long can be determined only through trial and error If flutter returns on a given dosage it indicates that after re version again is obtained a larger maintenance dose is necessary

In those cases that change from auricular flutter to auricular fibril lation on digitalis therapy, which subsequently do not become regular it becomes a matter of judgment whether to accept the fibrillation as per manent and to continue digitalis indefinitely or to use quinidine with the hope of producing a normal rhythm If the latter course is chosen quin idine is given in much the same way as has been outlined for the treat ment of persistent flutter It is obvious that the diagnosis of auricular flutter is not a simple matter and its treatment is complicated The treatment of such cases therefore requires hospitalization where exact changes may be followed with great care In most cases therapy is ef fective and in some it is of vital importance

Auricular Fibrillation

Auricular fibrillation is the most common important irregularity of the heart It is the condition that formerly had a variety of names i e delirium cordis absolute or total or gross irregularity of the heart per manent or perpetual arrhythmia By electrocardiographic study it was found to be due to a tumultuous rapid fibrillary state of the auricles in which the number of impulses ranged from 400 to 800 or more per min ute It resembles auricular flutter in that it results from a circus move ment in the auricles but the rate of the circus is more rapid and the pathway is irregular The auricles do not contract coordinately but rather remained distended in a diastolic state The junctional tissue cannot conduct such a great number of impulses from auricles to ven tricles and so the rate of the heart may be 100 120 150 or so The rhythm will be absolutely irregular quick beats and slow beats coming without predictable pattern The peripheral pulse also will be totally irregular in time and force Because some of the weaker ventricular contractions fail to reach the periphery there will be an appreciable pulse deficit i e the radial pulse rate will be distinctly less than the apex rate (Fig 15) A pulse deficit although very common in auric ular fibrillation is by no means pathognomonic of this condition as it will be found where there are numerous extrasystoles and in cases of auricular flutter or ventricular tachycardia when the heart rate is irreg ular and rapid

Auricular fibrillation although formerly called perpetual arrhythmia frequently occurs as transient paroxysms These may last a few hours or days When the irregularity continues uninterruptedly for more than a week it is very rare that a normal rhythm is resumed unless specific medication is given or unless a definite cause like hyperthyroidism can be removed As a permanent or transient arrhythmia it is frequent in rheumatic heart disease especially mitral stenosis hypertensive or coronary artery disease and thyrotoxicosis It is particularly prone to be paroxysmal in hyperthyroidism It is fairly common and almost always transient during the early days following an attack of acute coronary



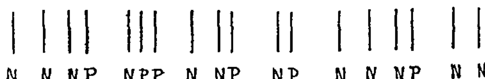
FIG 15 *Auricular impulses (A) are very numerous 500 ± Ventricular responses (V) are totally irregular rate about 150 Radial pulse (P) is irregular in time and force rate about 120 Note that some of the quick ventricular beats do not reach the radial pulse thereby producing a pulse deficit*

thrombosis It occasionally develops during pneumonia and rheumatic fever less commonly with other infections It is also met with in a variety of other conditions such as constrictive pericarditis beri beri heart following accidents etc There remains a group of patients which is by no means small in which auricular fibrillation either permanent or paroxysmal may be present without any other evidence of organic disease in the heart or elsewhere These may be called normal fibrillators It is evident that this arrhythmia is not only very common occurring as it does under a great variety of circumstances but from a practical point of view is very important

Diagnosis — The clinical bedside diagnosis in most cases is not difficult Before treatment is instituted the heart rate will be rapid over 100 the rhythm apparently grossly irregular the radial pulse varying in time and force and an appreciable pulse deficit will be present Under the above circumstances the diagnosis of auricular fibrillation will be correct nine times out of ten One can even be more certain if it is

known that the patient has mitral stenosis and there is a past history of rheumatic infection In fact the triad auricular fibrillation mitral stenosis and a rheumatic history is correlated so intimately that if two are known to exist the third quite surely is present

Occasionally numerous extrasystoles auricular flutter and other irregularities may simulate closely auricular fibrillation There are three additional points that may aid in differentiation The quality and intensity of the first heart sound in auricular fibrillation will not vary at all from cycle to cycle or only to such an extent as could be explained by the differences in the length of the heart cycle When ventricular



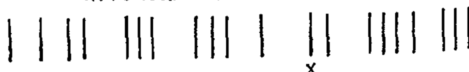


FIG 16 Upper graph shows several premature beats (P) preceded by normal beat (N) and followed by compensatory pauses Lower graph which superficially resembles the upper also shows quick and slow beats but at one point (X) a slow beat is not preceded by a quick beat This typifies auricular fibrillation

extrasystoles are present the first heart sound will change in character This will occur also in some cases of partial heart block with varying conduction time and in some instances of nodal rhythm The reason for this is that the changing relationship between auricular and ventricular systole alter the first heart sound The second point that distinguishes numerous extrasystoles from auricular fibrillation is that whereas both may appear to be grossly irregular with quick and slow beats coming tumultuously and both conditions may have short cycles followed by pauses only in the latter will pauses occur that are not preceded by quick beats With extrasystoles all long pauses are compensatory and follow a premature beat while with auricular fibrillation a long pause may follow a previous beat that is not short (Fig 16) This

generally can be detected on careful auscultation Finally extrasystoles generally disappear if the heart rate is increased by exercise or atropine while the gross irregularity persists if fibrillation is present

When the heart rate has been slowed previously by digitalis the *recognition of auricular fibrillation may be more difficult The irregularity will not appear as striking* and there may be no pulse deficit If this possibility is kept in mind the diagnosis may become clear if the heart rate is accelerated by exercise or by atropine Occasionally under full doses of digitalis a fibrillating heart may become perfectly regular Under such circumstances either a normal rhythm has been established or the *ventricles are beating regularly and independently* while the auricles are fibrillating *Generally it is necessary* to have electrocardiograms to distinguish these two conditions unless the presence of a presystolic murmur is detected from which one could infer that the auricles are contracting normally

Treatment — Digitalis is the drug of choice for auricular fibrillation The effect is specific and dramatic With adequate doses the heart rate may be expected to slow to within normal limits in most cases if heart failure is present unless there is thyrotoxicosis or fever and even then some slowing is likely to occur Although this is the condition in which digitalis gained its reputation as the most valuable drug in the treatment of heart failure it must not be inferred that it lacks beneficial effect *when fibrillation is absent It is now acknowledged* by most authorities that digitalis is indicated in the presence of congestive heart failure no matter what the rhythm may be It does not do away with the fibrillation This continues indefinitely It slows the ventricular rate and improves the efficiency of ventricular contraction If it is desired to stop fibrillation of the auricles and to produce a regular rhythm *quinidine is necessary*

Digitalis generally is administered by mouth but can be given rectally in liquid form When the situation is very critical and effects are necessary in minutes or hours intramuscular or intravenous injections may be given In the average case 3 to 5 pills each 0 1 gram (1½ grains) may be given daily for several days diminishing the dose as therapeutic or toxic effects appear After this the so called daily maintenance dose is given This may vary in different individuals from one half to two *tablets a day One must find out in each case what the optimum dose* will be It is important to appreciate that the strength of many preparations commonly used has increased in recent years Whereas in former *times patients often received too little digitalis partly* because some preparations were considerably below the expected potency now many

are being intoxicated by digitalis This can be avoided easily, if evidence of deleterious action is watched for, such as excessive slowing of the heart coupled beats nausea vomiting and yellow vision The numerous details concerning digitalis therapy the indications and the dosage for intravenous and intramuscular administration etc will not be gone into as they have been considered in other chapters

Quinidine — The indication for the use of quinidine in persistent auricular fibrillation is a very moot question In the majority of cases the drug can restore the regular heart beat by breaking up the abnormal circus movement There are several reasons that have prevented the general adoption of this treatment of auricular fibrillation and have cooled the original enthusiasm that characterized the early reports on its use Quinidine is a dangerous drug It can produce sudden unpredictable fatalities It does so by some direct toxic action on the heart, for it can inhibit impulse formation and it can produce respiratory depression By making the auricles contract that previously were fibrillating thrombi may be dislodged resulting in hemiplegia or other peripheral embolism Inasmuch as there is no method of foretelling whether mural thrombi are present until bits become dislodged such serious complications cannot be predicted Furthermore many cases of auricular fibrillation when made regular by quinidine revert to the previous gross irregularity after a few days or a few weeks despite medication Finally some patients are not any better or enough better after being made regular to warrant the risk involved For these reasons the use of quinidine in the treatment of persistent auricular fibrillation is quite limited It must be admitted that in the majority of instances the patient would be in better health with the heart beating regularly than with a grossly irregular rhythm If there were no risk involved therefore quinidine would be of great value As a practical matter it appears that most of the unfavorable or disastrous results from its use have occurred when given to cases of auricular fibrillation with mitral stenosis rather than to the non valvular fibrillators It may be concluded therefore that quinidine should not be given to persistent fibrillators who have mitral stenosis or should be given only in unusual circumstances fully aware of the possible dangers

Quinidine has a very useful place in cases of auricular fibrillation that have no other evidence of heart disease Here it is almost invariably effective in restoring the normal rhythm It is also effective in cases of hyperthyroidism one or two weeks after subtotal thyroidectomy when fibrillation persists despite the return of the basal metabolic rate to normal It may be used occasionally in hypertensive or other non valvular types of heart disease that have auricular fibrillation

Originally it was claimed that the most favorable cases were those in which cardiac enlargement is not marked congestive failure absent or only very slight and the irregularity of weeks or months rather than of years duration However I have had fatalities when all these favorable indications were present and striking successes when all the circumstances were just reversed It must be borne in mind that a physician is justified more completely in employing a dangerous procedure like quinidine therapy if the patient is doing poorly and the outlook otherwise hopeless than when he is still ambulatory doing tolerably well and likely to carry on for some years on a safer procedure like constant digitalization

When it has been decided to give quinidine sulfate for persistent auricular fibrillation the patient should be treated in a hospital and kept under careful observation All the methods customarily employed for congestive failure if present should be carried out Digitalis in appropriate doses should be given and diuretics if necessary to restore the circulation to the best possible state of compensation Then while continuing the daily maintenance dose of digitalis generally 0 1 or 1½ grains gradually increasing doses of quinidine are administered much in the same way as has been outlined already in the treatment of auricular flutter The first dose should be 0 2 gram (3 grains) At four hour intervals repeated doses may be given increasing the amount by 0 1 gram (1½ grains) with each dose or less rapidly depending on the urgency of the situation It is important to examine the patient before each dose of quinidine is given to ascertain whether the arrhythmia still is present It is obvious that an increase would be unwise if the heart had become regular following the previous dose At times it may be difficult to be certain without electrocardiograms whether fibrillation is still present For this reason such cases are best treated in a hospital If the normal regular rhythm is restored a maintenance dose of 0 2 to 0 3 grams (3 to 5 grains) of quinidine sulfate two or three times daily may be continued for some weeks or months or longer if it seems necessary

During the few days while increasing amounts of quinidine are being given evidence of toxic symptoms must be watched for Nausea vomiting diarrhea skin rash and buzzing in the ears may develop Although these are toxic manifestations they are not really harmful and quickly disappear if the drug is discontinued They need not always signify that the therapy should be stopped If syncope convulsions or significant respiratory distress occurs however quinidine therapy should be omitted entirely Liberal use of caffein intramuscularly or intravenously and even artificial respiration should be employed if sudden respiratory

distress develops Generally if the rhythm is to become regular, it will be obtained when doses of 0 5 gram to 0 7 gram (7½ to 10 grains) are reached Occasionally much larger doses have been necessary and effective It must be appreciated that quinidine in these larger doses is a cardiac poison and temporarily does harm to the heart It is therefore unwise to spend weeks in finding out whether it can make the heart regular or not At the end of several days the drug should be discontinued if it has been found ineffective, or should be reduced to a small maintenance dose because a regular rhythm has been obtained A common and serious error is to permit patients with auricular fibrillation to take both digitalis and quinidine daily for long periods of time Under these circumstances the quinidine makes it more difficult for digitalis to produce the desired slowing effect on the heart In other words quinidine should be given for only short periods of time to stop auricular fibrillation and should be omitted entirely if it fails to do so It is clear that quinidine therapy is not a simple matter and should not be undertaken except with full understanding of its intricacies

Nodal Extrasystoles

Extrasystoles may arise in the auriculo ventricular node or the bundle of His (Fig 7) They are not common and cannot be recognized readily without graphic tracings They have no specific significance and occur in normal individuals as well as in those suffering from any of the common forms of heart disease They are essentially harmless and do not require any therapy

Ventricular Extrasystoles

In considering ectopic rhythms starting in the auricles and going downwards in the heart it would be logical and sequential to consider ventricular extrasystoles at this point Inasmuch as auricular and ventricular extrasystoles have so much in common they naturally lend themselves to a combined discussion A consideration of ventricular extrasystoles will therefore be found in a preceding section Extrasystoles Premature or Ectopic Beats

Paroxysmal Ventricular Tachycardia

Ectopic beats may arise in any portion of the ventricles When they are isolated they are called ventricular extrasystoles If a series of

such beats arise in this same focus it is called a paroxysmal ventricular tachycardia These beats may continue uninterruptedly for seconds *minutes hours days or weeks* There is some reason to suspect that some attacks of ventricular tachycardia are due to a circus movement in the ventricles similar to the mechanism of auricular flutter or fibrillation in the auricles

This form of paroxysmal tachycardia is unlike the more common paroxysmal auricular tachycardia in many respects It occurs for the most part in patients who have grave heart disease although occasionally it appears without any evidence whatever of *organic disease* Generally it is associated with coronary sclerosis or thrombosis or with



FIG 17 Auricular rate is about 94 ventricular rate 206 Note that first eight cycles are perfectly regular followed by a few irregular beats and that the relationship between auricular and ventricular contraction varies

valvular disease of the heart Occasionally it appears as paroxysms just as in the case of auricular tachycardia and fibrillation It also occurs in cases in which electrocardiograms show a short P–R interval and a long QRS complex Both the auricular and ventricular forms of tachycardia may end spontaneously after minutes or hours although the latter is more apt to continue if not treated The heart rate is about the same in both ranging around 170 to 220

Diagnosis — There are several important differences that enable the physician to *identify* ventricular tachycardia at the *bedside in most instances* During the attack whereas auricular tachycardia is perfectly regular slight irregularities in rhythm may be detected on careful auscultation in many but not all instances of ventricular tachycardia Furthermore the quality and intensity of consecutive beats are all alike *in the former* while with the *latter* definite alterations in the heart sounds of some of the cycles are readily heard even when the rhythm is regular This results from the changing relationship between auricular and ventricular contractions (Fig 17) *Furthermore* various methods of producing vagal stimulation such as ocular or carotid sinus

pressure or deep breathing never produces any effect on ventricular but often stop auricular tachycardia Finally in some instances prominent auricular waves may be seen in the jugular pulse in cases of ventricular tachycardia

Treatment — As will be seen now the effect of treatment also helps to distinguish the two types of tachycardia Digitalis is not only useless in ventricular tachycardia but it will tend to perpetuate it and to increase further the rapid rate The most effective treatment is quinidine sulfate In most cases this will restore a normal rhythm The dose required will vary a great deal In some instances one or two 0 3 gram (5 grains) tablets orally may be sufficient while in others it may be necessary to increase the dose to 1 0 to 1 5 grams or more (15 to 22 grains) During quinidine therapy the ventricular rate almost always slows before normal rhythm is resumed This serves as a therapeutic guide and denotes that a partial effect is produced and that larger doses may cause further slowing with finally restoration of a normal mechanism Quinidine may be given intravenously in doses of 0 3 to 0 5 grams (5 to 7½ grains) *There is some danger in this procedure and it should* be given only as a last resort and then very slowly and diluted with 200 to 300 c c of normal saline solution

Quite recently magnesium sulfate in doses of 1 0 to 3 0 grams (15 to 45 grains) intravenously has been employed in the treatment of paroxysmal ventricular tachycardia Although experience with this treatment has not been great so far it merits consideration Likewise potassium salts such as potassium chloride 1 0 gram (15 grains) four times daily *by mouth have been recommended*

If paroxysms of ventricular tachycardia tend to recur the oral administration of quinidine sulfate 0 2 to 0 3 grams or more 3 to 5 grains two or three times a day may be useful In the rare case in which attacks may be predicted i e when they follow effort an appropriate dose one half to one hour beforehand may prevent the attack

The importance of recognizing paroxysmal ventricular tachycardia lies in the fact that digitalis the drug ordinarily used in heart disease is useless while other preparations especially quinidine may be effective and occasionally life saving

Ventricular Fibrillation

When fibrillation develops in the auricles see section 'Auricular Fibrillation the ventricles continue to contract although they do so tumultuously Blood flow continues and an adequate circulation may

be maintained for years When ventricular fibrillation develops on the other hand there is no contraction of the ventricles no output of blood and cessation of the circulation ensues If this continues for more than a few minutes death results This condition is observed very rarely in clinical medicine as it is only a fortuitous experience actually to make an electrocardiogram of such an event It can be produced easily in the experimental animal by applying a faradic current to the ventricles or by ligating a coronary artery It probably is a common cause of sudden death especially in patients with coronary artery disease although it is by no means the only mechanism in the production of sudden death Numerous cases have been reported in which electrocardiograms happened to be taken at the moment of sudden death which showed the mechanism to be ventricular fibrillation There are also rare instances in which repeated attacks of transient ventricular fibrillation occurred Such patients have spells of unconsciousness with recovery and some will show frequent ventricular extrasystoles or ventricular tachycardia just before the major attacks This can be recognized only by electrocardiograms There is reason to believe that quinidine therapy may help to alleviate this rare condition

Heart Block

In general there are two types of heart block The first is one in which block occurs between the sino auricular node and the auricles This is rare and comparatively unimportant In the second type the block takes place between the auricles and ventricles in the auriculo ventricular node or the bundle of His This type is common and important All types of heart block for the most part result from the same causes i e coronary artery disease myocardial and valvular disease of various forms digitalis administration and certain infections particularly rheumatic fever and diphtheria

Sino-auricular Heart Block

The normal regular heart beat arises in the sino auricular node and then spreads over both auricles When the impulse is blocked at its origin the condition is called sino-auricular block Under these circumstances neither auricles nor ventricles contract There is therefore a complete loss of a heart beat If only one such impulse is blocked the pause will be exactly twice the normal heart cycle Rarely the pause may be three times the duration of the normal interval when two im

pressure or deep breathing never produces any effect on ventricular but often stop auricular tachycardia. Finally in some instances prominent auricular waves may be seen in the jugular pulse in cases of ventricular tachycardia.

Treatment. — As will be seen now the effect of treatment also helps to distinguish the two types of tachycardia. Digitalis is not only useless in ventricular tachycardia but it will tend to perpetuate it and to increase further the rapid rate. The most effective treatment is quinidine sulfate. In most cases this will restore a normal rhythm. The dose required will vary a great deal. In some instances one or two 0.3 gram (5 grains) tablets orally may be sufficient, while in others it may be necessary to increase the dose to 1.0 to 1.5 grams or more (15 to 22 grains). During quinidine therapy the ventricular rate almost always slows before normal rhythm is resumed. This serves as a therapeutic guide and denotes that a partial effect is produced and that larger doses may cause further slowing with finally restoration of a normal mechanism. Quinidine may be given intravenously in doses of 0.3 to 0.5 grams (5 to 7½ grains). There is some danger in this procedure and it should be given only as a last resort and then very slowly and diluted with 200 to 300 c.c. of normal saline solution.

Quite recently magnesium sulfate in doses of 1.0 to 3.0 grams (15 to 45 grains) intravenously has been employed in the treatment of paroxysmal ventricular tachycardia. Although experience with this treatment has not been great so far, it merits consideration. Likewise potassium salts such as potassium chloride 1.0 gram (15 grains) four times daily by mouth have been recommended.

If paroxysms of ventricular tachycardia tend to recur, the oral administration of quinidine sulfate 0.2 to 0.3 grams or more, 3 to 5 grains two or three times a day may be useful. In the rare case in which attacks may be predicted, i.e. when they follow effort, an appropriate dose one half to one hour beforehand may prevent the attack.

The importance of recognizing paroxysmal ventricular tachycardia lies in the fact that digitalis, the drug ordinarily used in heart disease, is useless while other preparations, especially quinidine, may be effective and occasionally life saving.

VENTRICULAR FIBRILLATION

When fibrillation develops in the auricles (see section Auricular Fibrillation), the ventricles continue to contract although they do so tumultuously. Blood flow continues and an adequate circulation may

the ventricles the interval may be 0 24 or 0 3 seconds or more Arbitrarily it is regarded as delayed if the conduction time P-R interval is over 0 2 seconds In this condition there really is no true heart block for all beats do reach the ventricles but they are delayed constantly Therefore no irregularity in the rhythm will be detected on auscultation



FIG 19 Note that the line between auricular and ventricular contractions is prolonged This measures the conduction time of impulses between auricles and ventricles

It is difficult if not impossible to recognize this disturbance without graphic methods as the heart rate will be perfectly regular and need be neither abnormally rapid nor slow Generally it is first diagnosed by electrocardiograms There are two bedside findings however that may arouse one s suspicion and lead to the correct diagnosis Occasionally first degree heart block is associated with a gallop rhythm When the ordinary conditions in which a gallop rhythm is heard are lacking such as hypertensive or coronary artery disease especially when a gallop is found in a younger person who has or may have rheumatic fever or rheumatic carditis one should think of the possibility of first degree heart block The second point is a change in the intensity of the first heart sound The intensity of the first sound is loudest when *the conduction time is short about 0 08 to 0 10 seconds* and becomes fainter as the interval lengthens If the sound is heard to become less loud during the course of an illness or if it is found to be faint at the first examination the possibility of delayed conduction must be considered

Diagnosis — The diagnosis may be of considerable importance because whenever coronary artery disease or digitalis administration can be eliminated as possible causes it is a fairly reliable indication of acute myocarditis It is occasionally the only evidence in children of active rheumatic fever and always should make one suspect this diagnosis when other obvious causes are lacking Treatment is not directed at the heart block but rather at the underlying cause Atropine in full doses however may make it disappear temporarily

pulses are blocked. Such blocking of beats may take place only rarely or it may occur every few beats (Fig 18). It is very difficult at the bedside to distinguish this from the more common type of heart block to be discussed in the next section. It must be appreciated that inasmuch as neither auricles nor ventricles contract at the moment of block the usual 'a' wave that occurs in the jugular pulse will not be seen during the long pause while it may be detected in ordinary heart block.

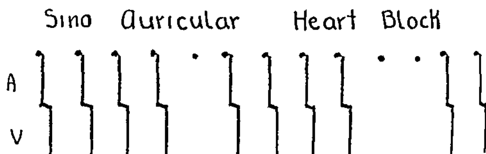


Fig 18. The dots indicate the formation of impulses of sino auricular node. Note *first the loss of one complete heart cycle and later of two consecutive heart cycles.* During the pauses neither auricles nor ventricles contract. The pauses are exact multiples of the length of the normal heart cycle.

Furthermore the duration of the pause is much more apt to be exactly twice the length of the normal cycle in sino auricular than in auriculo-ventricular block. In trying to make these determinations it is helpful for the examiner to tap his foot in rhythm with the regular heart beat and to continue the same rhythm during the pause. If the interval is twice the normal heart cycle the foot will come down *just on time* with the normal beat that follows the pause.

Ordinarily it is not necessary to treat sino auricular block as it produces no troublesome symptoms. When it is sufficiently marked it may cause palpitation, weakness, faintness or syncope and then the same treatment that is employed in ordinary heart block is indicated (see following section).

Auriculo Ventricular Block

First Degree Heart Block or Delayed Conduction Time

The earliest and mildest evidence of defect in conduction in the auriculo ventricular node or bundle of His junctional tissue consists of a delay in the passage of the impulse as it travels from auricle to ventricle (Fig 19). This is called first degree heart block or delayed conduction time. Instead of taking 0 14 to 0 20 seconds before reaching

It is not necessary to treat partial heart block but rather to direct attention to the underlying cause. When it is due to digitalis it is a sign of toxic action and serves as a warning to continue cautiously with the drug. No harm is done by the block. In fact the slowing of the ventricular rate that results may be beneficial but it does mean that large doses may be harmful. Furthermore the presence of any type of heart block when not the result of digitalis should not be regarded as a contraindication for the use of digitalis if the ordinary indication is present, i.e. congestive failure.

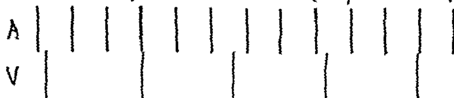


FIG. 21. Note complete independence of regular auricular rate of 89 and regular ventricular rate of 31.

Third Degree Heart Block or Complete Block. Adams Stokes Disease

When the degree of block at some point in the junctional tissue is complete and none of the impulses can reach the ventricles the circulation obviously would cease unless some other focus became the pacemaker to initiate contractions. There is an inherent automaticity in the ventricle to do this so that a point just below the region that is defective starts an idioventricular rhythm. This is normally slow, i.e. about 25 to 40 per minute. The auricles then are beating regularly in response to its pacemaker in the sino-auricular node while the ventricles are contracting independently in response to its pacemaker in the auriculo-ventricular node or junctional bundle. This complete dissociation is called third degree heart block (Fig. 21).

When the transition occurs between a normal rhythm or partial block to complete block there may be a temporary pause or asystole of the ventricle before its own pacemaker starts initiating impulses. Also when the heart is contracting at a rate of 32 there may be pauses of shorter or longer duration or the rate may fall to 10 or 15 per minute. These pauses or the undue slowing are responsible for the attacks of syncope or convulsions that characterize Adams Stokes disease.

Second Degree Heart Block or Partial Block

When the disturbance in conduction is more marked there is not only a delay in the passage of impulses but this gradually increases from beat to beat and finally one fails to get through and a ventricular contraction is lost (Fig 20) This is called second degree heart block or partial block This condition is not difficult to recognize for every now and then a pause in the heart s rhythm is detected This



FIG 20 Note that the interval between auricular and ventricular contractions gradually lengthens until one beat finally is blocked The ventricular pause is le s than two heart cycles because the following conduction time is short

may occur only at rare intervals or every fifth fourth or third beat It may be called 4 to 3 3 to 2 or 2 to 1 heart block indicating the relative number of auricular and ventricular beats Although the auricles continue to beat regularly there will be a loss of one complete ventricular cycle but the pause that takes place is not equal to two normal beats The reason for this is that just before the pause the conduction time is quite long and following the rest period it is quite short This makes the duration of the ventricular pause distinctly less than two normal heart cycles For the same reason the few beats before the block *generally are slightly faster than those* after the block

It is evident that in partial heart block some arrhythmia will be audible over the precordium This will at least direct attention to the possibility of heart block When there is 2 to 1 block however the rhythm obviously will be perfectly regular The auricular rate may be 90 and regular while the ventricular will be 45 and regular This might be misinterpreted easily as a normal bradycardia Occasionally one can hear faint auricular sounds over the precordium or see auricular waves in the jugular pulse during the long pauses which would identify the condition as heart block

must be made. Generally it is possible to hear faint auricular sounds to see additional auricular waves in the jugular pulse and occasionally to feel faint extra pulsations in the radial artery during the long pauses. These signs establish the fact that heart block is present and that it cannot be a normal bradycardia. The single finding that characterizes the condition as complete dissociation is the changing quality or intensity of the first heart sound and occasionally of the second sound. The first sound in different cycles may become faint or reduplicated or suddenly very loud. These alterations result from the constantly changing relationship between the time of auricular and ventricular systole and will not be present in any other condition (Fig 21). Another peculiarity of complete block but one that is of less value diagnostically is that the slow rate will be little influenced by deep breathing, vagal stimulation or effort.

Treatment — The treatment of complete block should be directed at the attacks of syncope. If no such spells occur there is no indication for medication unless congestive failure is present and then digitalis should be given. The severity of the symptoms during spells will depend on the duration of the asystole. If the heart stops for a few seconds the patient may merely feel a wave pass by or have a momentary feeling of weakness. If it lasts 5 to 10 seconds he will fall unconscious and quickly recover. If the pause is longer there will be convulsions and stertorous breathing and if it lasts more than a few minutes death results.

When spells are frequent coming many times daily the most effective remedy is adrenalin 0.3 to 0.5 c.c. of 1 to 1,000 solution subcutaneously every two hours. This plan is particularly applicable in cases such as acute coronary thrombosis when the entire emergency is not apt to last more than a day or two. When the condition is more chronic adrenalin in oil subcutaneously or 1 to 100 solution of adrenalin by throat spray may be employed. In some cases ephedrine sulphate 25 to 50 mgm (3/8 to 3/4 grain) three or four times a day orally may help to prevent attacks from recurring. Of less value is barium chloride 30 mgm (1/2 grain) four times daily or atropine sulfate 1 mgm (1/60 grain) three times daily by mouth. Occasionally digitalis appears to be of value in stabilizing the heart rate and preventing attacks of asystole. This may be of use when the degree of heart block seems to be related to the auricular rate. Prolonged thyroid therapy has been employed also at times with satisfactory results. When attacks occur only at such rare intervals as several months or a year or two it is difficult to institute or to appraise the value of treatment.

Complete block most commonly is associated with coronary artery disease It may be a gradual development following a period when only first or second degree block was present, or when there was only bundle branch block However it may appear suddenly without previous evidence of any conduction disturbance At times it is transient in the sense that directly before and after a spell conduction may be normal Occasionally it is present for a day or so after the onset of an attack of acute coronary thrombosis with myocardial infarction especially of the posterior type There are many instances in which complete block develops in patients past middle life without any previous evidence of cardiovascular disease possibly with the exception of hypertension There are some cases occurring in the fourth or fifth decades without any known etiology There is a suspicion that such cases may be related to a previous severe attack of diphtheria Aortic or mitral stenosis rheumatic in origin and syphilitic heart disease occasionally seem to be the causative factors There is a rare form of congenital complete block and then it may be associated with a defect in the upper portion of the ventricular septum There are also rare cases where it is due to a localized lesion such as an abscess perforation or gumma involving the bundle of His Finally complete block may result from digitalis intoxication but then the ventricular rate is more likely to be 50 to 70 or more rather than the customary rate of 30 The higher rates also are observed in children and in a few adults when the block is not the result of digitalis

Complete heart block may be temporary or permanent Some cases continue for many years without any symptoms and others have rare or frequent attacks of Adams Stokes syncope There is no satisfactory method of predicting when such attacks will occur how severe they will be or whether they will be fatal It is important to appreciate that when the heart is beating regularly and slowly at a rate of 30 to 40 the circulation may be quite normal Patients have been able to carry on doing strenuous work for many years with such slow rates In fact congestive failure is not common with complete block The main difficulty is not the slow steady rate but the tendency for the beat to stop entirely When such an asystole occurs death results if the beat is not resumed within a few minutes It is therefore the Adams Stokes attacks that mainly concern us

Diagnosis — The bedside diagnosis of complete block usually is not difficult There are few other conditions that are associated with such a slow regular heart When the rate is over 35 and particularly over 40 then its differentiation from a normal bradycardia or a 2 to 1 heart block

The pressure should be maintained for several seconds at about the systolic level in order to be certain whether such alternation is continuous and real and not dependent on breathing or on a decrease in pressure within the cuff In some cases the difference in strength of the two consecutive beats is so great that only the stronger beat will be heard until the pressure is lowered 10 mm of Hg or more when both become audible At this point though all sounds come through alternation will be evident Pseudo alternation may result when there is bigeminy Under these circumstances because every second beat comes prematurely it is also a weaker contraction The difference is that in pulsus alternans the weaker beat is not premature In the early stages alternation may be present only for six or eight cycles following an extrasystole Ordinarily there is no evidence of this condition to be obtained by auscultation or electrocardiography Occasionally however one can detect alternation in the loudness of the sounds of the heart or in the murmurs that may be present or in the strength of the apex impulse There are rare instances in which alternation in the amplitude of the QRS waves of the electrocardiogram are present and this has the same clinical significance as alternation of the pulse

Pulsus alternans is thought to be due to some disturbance in the contractibility of the ventricular musculature as if certain fibers fail to enter into systole until an additional rest period is obtained It is a fairly reliable sign of grave heart muscle disease and therefore carries a serious prognosis When found while the heart is beating very rapidly however such as during a paroxysm of tachycardia it does not have any ominous significance Because of its prognostic importance it should be sought for routinely while making blood pressure determination in all patients who have or may be suspected of having cardiovascular disease

There is no treatment for pulsus alternans Its importance lies in the fact that it denotes a grave disturbance of the heart muscle and thereby directs our attention to the underlying cause

CONCLUSION

The detection and proper interpretation of cardiac irregularities generally is possible with simple bedside methods Only in a minority of instances will graphic tracings be necessary The subject is important because in many instances the correct diagnosis of the arrhythmia may be the first or only clue available in directing attention at the underlying disease In other cases the irregularity itself is a serious handicap

One would have to continue a constant daily regimen for a long time in the hope of preventing this rare unpredictable attack

Bundle Branch Block

In considering arrhythmias or disturbances in the mechanism of the heart beat it is customary to include bundle branch block The impulse may be conducted normally through the auricles auriculo ventricular node and bundle of His and then be *blocked in the right or left branch* of this bundle The ventricles do contract regularly only very slightly

Pulsus Alternans



Fig 22 Note alternate small and larger waves obtained in a tracing of the radial pulse The rhythm however is perfectly regular

asynchronously There will therefore be no arrhythmia One cannot detect this condition clinically It can be recognized only by electrocardiograms which show very characteristic changes The only indirect bedside clue will be the detection of a gallop rhythm or a reduplicated *apex impulse These findings so often are associated with* bundle branch block that one should suspect the presence of the latter when the former are found It is of considerable importance for it denotes some structural disease of the myocardium and often but not always denotes a grave prognosis Treatment should be directed at the underlying condition and not at the bundle branch block

Pulsus Alternans

There is finally one peculiar disturbance of the heart beat that is not associated with any irregularity in rhythm It consists of an alternation in the strength of consecutive cycles and is called pulsus alternans (Fig 22) This term is only applicable for beats that come regularly and must be distinguished from pulsus bigeminus On palpating the radial pulse a stronger and weaker beat in regular sequence is felt It is even easier to detect this condition while taking the blood pressure As the cuff is blown up and the pressure allowed to fall when the *first sounds* appear at the systolic level they will be found to alternate in intensity

CHAPTER XI A

CLINICAL ELECTROCARDIOGRAPHY *

By FRANCIS F. ROSENBAUM

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* For a clinical discussion of cardiac arrhythmias see the preceding chapter, Chapt XI, The Clinical Aspects of Cardiac Arrhythmias, by Samuel A. Levine.

and if uncontrolled may lead to grave disability or death For the most part serious irregularities of the heart can be controlled or cured by proper medication when correctly diagnosed In many other instances the intelligent recognition of benign irregularities enables the physician to avoid making the diagnosis of organic heart disease when no disease is present

March 1 1942

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INTRODUCTION

The clinician who deals with problems concerning the heart has come to look upon the electrocardiograph as an increasingly useful adjunct to the diagnostic techniques available to him. Although in its early development the electrocardiographic method was considered most valuable in the study of the cardiac arrhythmias, in the past two decades there has been a growing appreciation of the significance of changes in the form of the electrocardiogram and the information thus afforded which is not otherwise available. The physician who utilizes the electrocardiograph must be aware not only of its potentialities but also of its limitations. The physicochemical phenomena responsible for the action currents of the heart which are recorded by this method are only indirectly related to the mechanical activity of the heart. It must be understood that the electrocardiogram is therefore no measure of cardiac function or reserve. The record may be normal in a patient who has marked congestive heart failure, or it may be distinctly abnormal in an individual who has no clinical evidence of diminution in the functional

capacity of the heart The standards for the normal electrocardiogram which are now available, still are incomplete and we are confronted frequently by records showing minor deviations of uncertain significance Although such variations ultimately may prove to be of some importance in the light of our present knowledge undue emphasis upon them may lead to unwarranted concern to the patient and his doctor

A number of general categories may be outlined as the types of cases in which the electrocardiograms may be of value (1) In the understanding and differentiation of the various cardiac arrhythmias the electrocardiogram has often been considered the court of final appeal For example our current views regarding the various types of paroxysmal rapid heart action circus rhythm and bradycardia stem largely from electrocardiographic observations such as those of Lewis and his associates[1] (2) Electrocardiographic studies are helpful in controlling certain cardiac medications particularly digitalis and quinidine Not infrequently records suggesting definite digitalis intoxication are obtained in patients who have no clinical or subjective manifestations of excessive digitalization When quinidine is used to control paroxysmal ventricular tachycardia or paroxysmal auricular fibrillation electrocardiographic control is advisable almost always (3) Some valvular lesions such as mitral stenosis produce electrocardiographic changes although usually only when the lesion is an advanced one Information which is helpful in differentiating various anomalies such as patent ductus arteriosus pulmonary stenosis or aortic stenosis is obtained often (4) The electrocardiogram is particularly useful in the detection of myocardial changes especially in those patients who demonstrate little other objective evidence of cardiac involvement In general these patients fall into two groups (a) those individuals with myocardial involvement usually transitory complicating some acute illness such as rheumatic fever scarlet fever diphtheria or pneumonia and (b) those cases with more chronic myocardial changes usually resulting from coronary arterial disease (5) Finally the electrocardiogram may disclose supplementary information of great interest in a wide variety of conditions such as hypertension acute pulmonary embolism beri beri myxedema acute pericarditis hyperkaliemia (hyperpotassemia) hypopotassemia hypocalcemia and hyperthyroidism

The electrocardiogram with only rare exception, does not make possible etiological diagnoses For example graphic signs of myocardial changes are observed which may be produced by any one of a large group of disturbances including coronary arteriosclerosis coronary

embolism syphilis disseminated vascular disorders or some drug therapy The characteristic picture of acute myocardial infarction and the typical transient changes recorded during attacks of angina pectoris are among the chief exceptions in which it is possible to express the opinion that the underlying disorder is one involving the coronary arteries and in all likelihood that it is due to coronary arteriosclerosis For the most part to consider less distinctive evidence indicative of coronary disease or coronary sclerosis is a dangerous practice and will tend ultimately to discredit the electrocardiographic method

The electrocardiograph records the electrical activity of the heart during the spread of the impulse of activation (depolarization) and its retreat (repolarization) over the auricular musculature through the specialized conduction system and over the ventricular myocardium The action currents developed by the heart are alternating current voltages which are in the range of 0 1 millivolt or more The recording instrument must possess therefore a high sensitivity and a small inertia These requirements are met by using a very fine conducting string in a powerful magnetic field in the case of the string galvanometer and a conducting *coil in a similar field but with amplification of the electrical current from* the heart in the case of the amplifier oscillograph type of instrument In each case as current passes through the conductor the lines of force about it are changed in such a way as to cause the conductor to be deflected to one side or the other of the resting position By means of a light source and an optical system this deflection can be magnified and recorded upon a moving sensitized film or paper Devices for registering time intervals and markings for measurement of the size of the deflections also are incorporated in the instruments The fundamental principles of the instruments available have been discussed in detail by Johnston Recently there have become available direct writing instruments which inscribe directly upon special recording paper the movements of a light weight recording arm with a heated wire tip The type of machine chosen should meet the individual requirements and situation of the user

A properly recorded electrocardiogram must meet certain technical requirements The instrument must be properly standardized so that 1 millivolt introduced into the circuit causes the string or light beam to be deflected 1 centimeter This is done in order that records on the same patient taken at any time may be comparable and to establish some basis for comparison of all electrocardiographic records The lead cables from the machine must go to the proper extremities the accidental interchange of these wires may result in reversal of the polarities which were orig

inally selected by Einthoven and are generally accepted. Muscle tremor may introduce many fine, irregular vibrations; this is seen frequently in hyperthyroidism and Parkinsonism. Gross muscle movements tend to produce larger, slower deviations of the record from the baseline. Stray, alternating current interference is manifest by rapid, regular, uniform vibrations of the baseline; it will occur when electric light cables or electrical equipment are placed near the patient. It usually can be eliminated by taking precautions with such alternating current apparatus and by properly grounding the recording instrument and occasionally the bed or table upon which the patient is lying. Overshooting is an artifact which tends to make the deflections larger than they should be. It will be noted when the string shadow fails to stop abruptly at the proper 1 cm distance when 1 millivolt is introduced but instead continues to travel a short distance beyond. It is seen usually when the skin surface is improperly prepared and especially in patients whose skin is dry or thickened. The sensitivity of the instrument should be such that when 1 millivolt is introduced into the circuit the string moves exactly 1 centimeter and assumes this position in 0.02 seconds or less. If the speed of response is slower than this limit the deflections will be smaller than they should be and the finer quicker oscillations may be completely obscured. This artifact usually occurs when the resistance in the circuit is too high, as when the skin surfaces beneath the electrodes are improperly prepared. It is important that the physician who undertakes to interpret electrocardiograms makes himself familiar with the artifacts which may occur in order that he may recognize them and understand something of their significance and origin.

The heart is believed to possess specialized tissues that initiate the stimulus which causes it to beat and which conduct this impulse to the cardiac musculature. Some of these structures can be seen grossly in the hearts of cattle, dogs and other mammals. There is some disagreement concerning their existence in the animal and human heart[3,4,5] but the similarity of experimental and human bundle branch block[6], the occurrence of such disturbances as partial bundle branch block[7] as well as other observations[8,9] make it probable that a comparable functioning system does exist in the human. The cardiac impulse is generally considered to originate in the sino-auricular node (Keith-Flack), which is imbedded high in the right auricle at the junction of the superior vena cava and the right auricle. This center usually is the pacemaker because it has an inherent rhythmicity and rate which are faster than those of other potential centers in the heart. The impulse leaves the sino-auricular

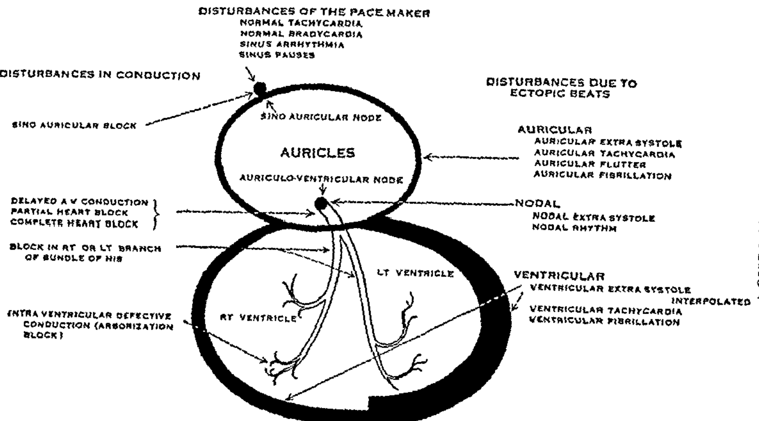


Fig 2 A diagram illustrating the relationships of the specialized cardiac conduction tissues and the sites of origin of the common disorders of the heart beat (From former chapter by Samuel A Levine in the Oxford Loose Leaf Medicine Vol II)

node to spread through the auricle in a radial fashion much like the spread of fluid poured on a flat surface" No specialized conducting tissues have been demonstrated in the auricular musculature The impulse leaves the auricle to enter the atrioventricular node (Tawara) which is imbedded somewhat posteriorly at the base of the auricular septum near the coronary sinus The impulse travels from the atrioventricular node through the main stem of the His bundle which extends from the lower end of the node to the top of the muscular portion of the interventricular septum At this point the His bundle divides into its right and left branches which in turn run beneath the septal endocardium to reach the Purkinje network This network extends its complex ramifications throughout the subendocardial aspects of both ventricles Thus a mechanism is present whereby the impulse can spread rapidly from the His bundle to the subendocardial musculature of both ventricles, thereby activating both of them practically simultaneously Inasmuch as the spread of the impulse is from within outward the thickness of the ventricular walls is an important factor in determining the time of arrival of the wave of activation at the epicardial surface It is believed that if the continuity of one of the bundle branches is interrupted the impulse travels down the intact bundle branch and through the septal musculature to reach the Purkinje network on the blocked side It is well to keep this system in mind as a background for the understanding of some of the disturbances of rhythm and alterations in the form of the electrocardiogram which will be discussed The illustrations shown in Figs 1 and 2 may serve to demonstrate this system more graphically Space does not permit extensive consideration of the nature of the origin and distribution of the electrical forces in the mammalian heart and the reader is referred to the works of *Waller*[10] *Craib*[11] *Einthoven*[1] Lewis[12] and Wilson[14] for discussions of physicochemical phenomena associated with depolarization and repolarization of the myocardium

ELEMENTS IN THE ELECTROCARDIOGRAM

The electrocardiogram consists of a series of deflections which have been designated by the symbols P Ta QRS T and U (Fig 3) The application of these designations recently has been standardized, particularly as they apply to the QRS complex[1] The first deflection in the cardiac cycle is the P wave It is a small, rounded elevation which represents the spread of the impulse over the auricle The P wave is normally

no taller than 2 5 to 3 0 mm in any lead and no greater than 0 08 to 0 10 seconds in duration The P waves normally are upright in Leads I and II but may be upright diphasic or inverted in Lead III The P wave is



Fig 2 A photograph of the left branch of the His bundle its branches and the ramifications of the Purkinje network in the heart [illegible] The His bundle was injected with a barium mixture (From an article by F N Wilson)

followed by a small downward Ta wave which represents repolarization of the auricle this deflection usually is superimposed upon and therefore obscured by the QRS complex except in instances of marked prolonga

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where the deflection reaches its maximal elevation downward deflections are measured from the lower edge of the trace at the beginning of the QRS interval to the lower edge of the trace at its maximal depression It has been recommended that the components of the QRS complex be labeled in the following manner[2] The earliest deflection which lies

TABLE I

	P		Q		R		S		T	
Lead	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max
			0	1 5	1 5	1 ?4	0	5.0	1.0	5 5
I	0	1 1	0	.0	1	0	0	6.0	−0 5	5 ?
			0	2.0	4.0	.0	0	8.0	1.0	6.0
II	0 3	5	0	5	4.0	3 0	0	0.0	0.0	8.0
			0	.0	?	8	0	?.0	0	?.0
III	−1.0	2.0	0	3 [illegible]	1.0	0.0	0	[illegible]	2 [illegible]	5 5
V [illegible]			0	7 [illegible]	0	3.0	0	10 5	−3 3	−0 8
V			0	1 ?	0	[illegible]	0	.0	− .0	.0
V			0	2	0	13 0	0	6 5	0 2	2 8
V			0	0	.0	9 [illegible]	3.4	4	−4.0	? [illegible]
V			0	0	4.0	0 8	3.0	38.8	2.4	1 .0
V [illegible]			0	0.4	6.0	34 [illegible]	0	12.0	3.6	12.0
V			0	3.0	[illegible] 2	4 [illegible]	0	16.0	4	1 .0
V			0	3.4	8.8	33.0	0	9.6	2.0	9.6
V (ensiform)			0	0	2.0	1 8		6 2	0	6 2

Values in upper rows for leads I II and III and those for all other leads from Johnston and Kossmann [1]

Values in lower row for lead I II and III from Ashman and Hull[18]

above the reference level is the R wave any downward deflection which *precedes* R is designated a Q wave whereas any downward deflection which *follows* R is labeled S the first upward deflection which follows S is labeled R and the first downward deflection which may follow R is called S should succeeding deflections occur they are labeled R S and so on If no R wave is present the single downward deflection which occurs is labeled QS One deflection ends and a second deflection begins only when the trace crosses the reference level A deflection is notched when it displays more than a single turning point before crossing the reference level a deflection is slurred when it

tion of auriculoventricular conduction or complete atrioventricular heart block The Ta wave is of little clinical significance

The QRS complex or initial ventricular deflection represents the spread of the impulse over the ventricle as it is passing into the active state The normal limits of the size of the individual deflections of this

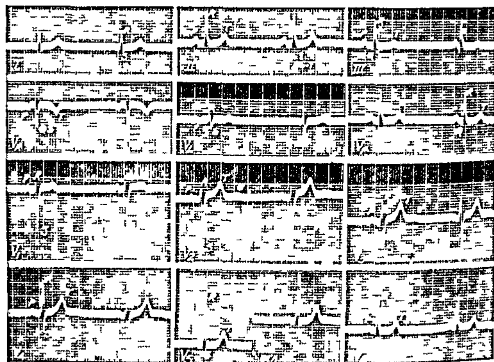


Fig 3 Normal standard and unipolar limb leads and multiple precordial leads in a woman aged 37 years who had no heart disease The various deflections have been labelled Prominent U waves are seen in leads V_2 and V A proper standardization is shown in lead V indicated at STA

group in the electrocardiographic leads commonly employed are given in Table I If the largest deflection in this complex in any of the standard leads exceeds 24 mm the deflections are said to be abnormally large If the largest deflection in any of the standard leads is 5 mm or less the deflections are considered abnormally small In making measurements and assigning symbols to the deflections the reference point is that level from which the first deflection in the QRS complex begins Upward deflections are measured from the upper edge of the trace at the beginning of the QRS interval to the upper edge of the trace at the point

lines are at twice the usual distance apart this is merely the result of increasing the camera speed to twice the normal rate and does not affect the actual duration of the time intervals Since each vertical line represents 0 04 sec there are 1 500 fine lines and 300 heavy lines per minute If the cardiac rhythm is regular it is possible to measure the heart rate by merely selecting a prominent deflection in the tracing and counting the number of time lines to the point at which that same deflection next occurs Thus if a single cycle encompasses twenty small divisions the heart rate is $\frac{1\,500}{0} = 75$ per minute If the cardiac rhythm is irregular the number of R R intervals over a considerable portion of the record can be counted and then after determining the number of 0 04 sec or 0 20 sec intervals encompassed the rate can be determined from either of these formulae

$$(1)\ \frac{\text{Number of R R intervals} \times 300}{\text{Number of 0 0 sec intervals encompassed}} = \textit{Rate per min}$$

or

$$(2)\ \frac{\text{Number of R R intervals} \times 1\,500}{\text{Number of 0 04 sec intervals encompassed}} = \text{Rate per min}$$

In measuring the intervals in the electrocardiogram it is the best general practice to take the longest interval as it occurs in any lead or the mean of the intervals in the two leads in which the measurements are most nearly equal It is well to avoid using that lead in which the given interval is shortest since the direction of the average spread of activation *the mean electrical axis* may be perpendicular to that particular lead resulting in an isoelectric period at the beginning or end of the given interval Ashman and Hull[16] recommend measuring the P R interval in that lead in which P is highest it is often a good practice to measure all of the intervals in that lead in which the deflections are largest

The *P R interval* is measured from the *beginning of the P wave* to the beginning of the first deflection of the QRS complex It is a measure of the time it takes the activating impulse to travel from the sino auricular node over the auricle through the atrioventricular node down the His bundle and its branches and then to depolarize a sufficient amount of ventricular muscle to initiate the earliest QRS deflection The P R

displays a local thickening on either limb or at its peak The T wave or final ventricular deflection represents the repolarization of the ventricle It is not opposite in form and direction from the QRS complex, because the recovery process extends over a longer time and the duration of systole is not equal in all parts of the ventricular musculature Except in rare instances the T wave is normally upright in Leads I and II but it may be upright, inverted or diphasic in Lead III The T wave usually is less than 6 mm in height in the standard leads T waves are said to be diphasic when they display two distinct turning points one on each side of the reference level Occasionally a small rounded deflection occurs shortly after the T wave This is designated as a U wave and is believed to represent some readjustment of the polarization of the ventricular muscle although its significance is uncertain The U wave tends to be particularly prominent in records taken over the right precordial area

It has been recommended[1] that the term RS T junction (sometimes labeled J) be used to indicate the point at which the QRS complex end and the more gradual slopes of the T wave begin The level of reference used for measurement of displacement of the RS-T junction is the same as that which is used for measurement of the QRS complexes It may be displaced upward (high take-off') or depressed (low take off) The term RS-T segment is applied to that part of the ventricular complex, which immediately follows the RS T junction particularly in those records in which the RS T junction is followed by a flat or gently sloping tracing which ends with the onset of a steeper slope rising or falling to the apex of the T wave If this portion of the trace shows no sharp changes in contour it is more properly called the first limb of the T wave

Intervals of the Electrocardiogram

The horizontal markings shown on most electrocardiograms are so arranged that the lines are 0 1 cm apart and every fifth line is somewhat broader to facilitate measurements The vertical markings represent time intervals and usually are so inscribed that each vertical line represents 0 04 sec every fifth line is somewhat broader, and the interval between two heavy vertical lines is therefore 0 20 sec The speed at which the recording film or paper travels through the camera usually is independent of these time markings Therefore although in some of the figures which will be used in succeeding portions of this discussion the time

method are very similar to those of Bazett The Q T interval becomes prolonged particularly in those disorders accompanied by a low ionic blood calcium level especially uremia hypoparathyroidism and alkalosis as in prolonged vomiting and hyperventilation It may be prolonged also in hypopotassemia myocardial infarction and in refrigeration therapy[18] Shortened Q T intervals may be seen in hyperparathyroidism and after digitalis[19] It has been observed that although mechanical and electrical systole usually vary together this is not always true and in some cases of hypocalcemia mechanical systole may be of normal duration even though the Q T interval is much prolonged[8]

Einthoven's Law and the Einthoven Triangle

The electrocardiograph measures the difference in potential between two points on the body The standard leads were so selected by Einthoven that Lead I is a record of the potential difference between the left arm and the right arm ($V_L^* - V_R$) Lead II is a record of that between the left leg and right arm ($V_F - V_R$) and Lead III is a record of that between the left leg and left arm ($V_F - V_L$) All points on any one of the extremities have been found to display the same potential variations throughout the cardiac cycle[1] When the standard leads are taken the extremities behave much as if they were extensions of the lead wires from the galvanometer to the points of attachment of the arms and left leg to the trunk Such leading has the great advantages of convenience and ease of reproduction

Einthoven[2] set forth an expression concerning the relation of the standard leads to each other which has become known as Einthoven's law He stated that at any given instant in the cardiac cycle the sum of the deflections in Leads I and III must equal the deflection in Lead II It must be borne in mind when applying this law that it does not mean that the R wave or any other given deflection in Lead I plus that in Lead III will equal always the height of the R wave in Lead II using the maximum height of each in the respective leads since that maximum amplitude may not be reached at the same instant in all three leads that is the peaks of the R waves may not be in phase This law has many useful applications among them the detection of technical errors in recording the electrocardiogram

* The symbol V is used here to indicate potential

interval grows longer with increasing age and apparently with increase in the body length. The normal range for the P-R interval in adults is 0.12 to 0.20 sec. The range in infants and children is 0.08 to 0.16 sec. The length of the P-R interval tends to vary inversely with the heart rate so long as the variation in rate is due to decreased or increased vagal tone. The pathway for the impulse in the auricle is so broad that an isolated lesion in that chamber will not affect the P-R interval. The pathway for the impulse in the atrioventricular node and His bundle is narrow, and an isolated lesion here easily may impede the spread of activation. Consequently, when the P-R interval is found to be prolonged, the lengthening usually may be attributed to delay in the atrioventricular node or His bundle.

The QRS interval is measured from the beginning of the initial deflection to the end of the final deflection of the QRS complex. This interval is a measure of the time required to activate completely the ventricular myocardium. The normal range of its length in adults is 0.06 to 0.10 sec., whereas the range is from 0.045 sec. in infants to 0.09 sec. in older children[16]. Since the ramifications of the Purkinje network are very extensive, prolongation of the QRS interval usually is the result of delay in impulse transmission in the bundle branches. However, occasionally depression or involvement of the Purkinje tissue may be extensive enough to be responsible. Prolongation of the QRS interval usually is spoken of as intraventricular block. In the majority of instances the electrocardiographic evidence makes it possible to indicate in which of the bundle branches the delay is occurring and to classify the case as right or left bundle branch block.

The Q-T interval is a measure of the time from the initial activation of the ventricles to their return to the resting repolarized state, i.e., electrical systole. This interval is measured from the beginning of the QRS complex to the end of the T wave. Since the Q-T interval varies greatly with the heart rate, a number of formulae have been offered which employ the cycle length as a factor. Bazett[17] recommends the formula

$$K = \frac{\text{Q-T interval (as measured in seconds)}}{\sqrt{\text{R-R (cycle length in seconds)}}}$$

By this method the range of normal for K is 0.36 to 0.42 with the average for males 0.374 and for females 0.388. Ashman and Hull[18] have proposed the formula $QT = K [\log (c + l)]$ where l is a constant equal to 0.07 sec. and c is the cycle length in seconds. The values for K by this

heart Our greatest advances in the correct diagnosis of the disorders of the heart beat came with the development of graphic methods particularly the polygraph of Mackenzie and the electrocardiograph Because of its convenience and its greater ease of application the latter is now the chief clinical instrument employed in the observation of arrhythmias and the study of those which are not at once clear at the bedside In fact the ease and accuracy with which experienced observers are able to recognize the various disorders of the heart beat the bedside usually stems from considerable practice in correlating observations of the pulse and auscultation of the heart with study of electrocardiograms in the same patients Wilson classified the disorders of the heart beat into five major categories (1) those disorders due to variations in the rate the rhythm and the location of normal impulse formation (2) heart block (3) those disorders due to abnormal impulse formation (4) those disturbances due to circus rhythm and (5) pulsus alternans With the exception of this final category this classification will be used as the framework of the present discussion *

The cardiac musculature is peculiar in that it generates spontaneously the impulse to which it responds The specialized conduction tissues which already have been described briefly possess the property of forming normal rhythmic impulses Rhythms arising in centers located in these tissues are called *homogenetic rhythms* in contradistinction to those arising in other parts of the heart and which are called *ectopic* or *heterogenetic rhythms* The sino auricular node exhibits this ability to generate impulses to a greater degree than any of the other specialized tissues it is therefore usually the cardiac pacemaker As each impulse from this pacemaker travels through the conduction system it destroys any incipient impulses which may be developing at other points In the sino auricular node itself the cephalic end of the structure appears to possess the fastest inherent rate The rate of development of impulses in these special tissues apparently is influenced by nervous and physicochemical stimuli Vagal stimulation tends to decrease the rate of impulse formation in the sino auricular mode and apparently drives the pacemaker down to a lower level in the node On the other hand sympathetic stimulation accelerates the rate of impulse formation and the pacemaker moves toward the cephalic end of the sino auricular node Such manifestations

* The author is indebted to Dr Frank N Wilson for his permission to use many of the figures originally published in his article on this subject much of the material *in this discussion is drawn from that article as well as from the publications of Lewis* and Levine

Einthoven and his associates [3] described in 1913 a method whereby it was possible to determine from the standard leads the "manifest" value and direction of the resultant electromotive force produced by the heart at any instant in the cardiac cycle. It was postulated that the heart could be considered a small region at the center of a sphere and that the attachments of the three extremities used in taking the standard leads could then be considered the apices of an equilateral triangle with points at the surface of the sphere and lying on a plane passing through the center of the sphere. This triangle has been called the Einthoven triangle. The principle to be valid depends upon several assumptions including (a) the homogenity of the body tissues as electrical conductors, (b) the equidistance from the heart of the attachment of the extremities to the trunk and (c) the situation of these attachments at the apices of an equilateral triangle. Some writers[21] have questioned its validity, but Wilson[2, 6] has expressed the opinion that although these assumptions are not strictly in accord with the facts the errors introduced are too small to invalidate the method for practical purposes. Since the standard leads form the three sides of Einthoven's equilateral triangle with the heart at the center, using the triangle as the basic construction one can determine the pattern in the standard leads which will result from a force of any magnitude or direction. Conversely, given the standard electrocardiogram, it is usually possible by projecting the deflections of any two of the standard leads toward the center of the triangle to determine the mean electrical axis. This point will be discussed in greater detail when the subject of deviation of the mean electrical axis and ventricular hypertrophy is considered.

DISORDERS OF THE HEART BEAT

Introduction

The recognition and management of disturbances of the cardiac rhythm make up an important segment of cardiological practice. Such disorders are derangements of function, which may occur in many disease states and are not necessarily associated with demonstrable anatomical abnormalities. These disturbances must be diagnosed accurately in order that they may be evaluated properly, related to any other cardiac abnormalities which may be present and treated correctly. It no longer suffices to label a disturbance of cardiac rhythm as simply an irregular

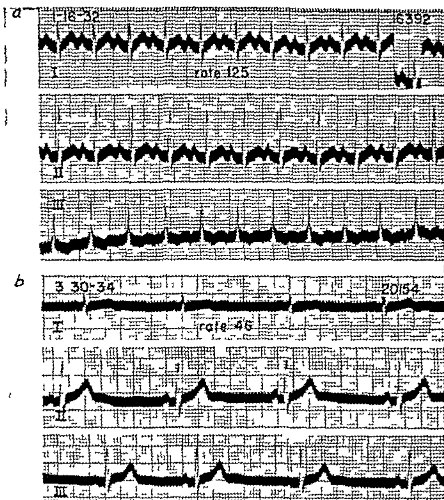


FIG 4a Sinus tachycardia This record was taken from a pregnant woman aged 19, who had an exophthalmic goiter The basal metabolic rate was plus 62% A thyroidectomy was performed one month after this electrocardiogram was made Inverted T waves such as are present here in lead III occur in many normal patients

FIG 4b Sinus bradycardia This electrocardiogram is that of a man aged 19 who was admitted to the hospital with acute diarrhea The examination was negative except for the slow heart rate The record is of normal outline the sole abnormality is the bradycardia

stress or exercise In these individuals the rate rises to unexpectedly high levels and remains elevated longer than is the case in normal persons

as the slowing of the heart, which occurs with distention of the visceral pleura (Hering-Breuer reflex), and the acceleration, which appears with distention of the great veins in the neck (Bainbridge reflex) suggest that reflex stimuli influence the cardiac pacemaker The range of the normal heart rate is considered to be 60 to 100 beats per minute To be significant the heart rate must be determined in a basal state so far as is possible since it is influenced very easily by emotion excitement, fatigue and other similar stresses

Sinus Tachycardia

Sinus tachycardia is a disorder in which the sole abnormality is an increase in the rate of impulse formation in the sino-auricular node above 100 beats per minute This rhythmic disorder itself does not alter the form of the electrocardiogram The P waves almost invariably are seen and usually are large particularly in Leads II and III This increase in the height of the P waves is the result of the displacement of the pacemaker to the head of the sino-auricular node the spread of the impulse over the auricle is therefore in more nearly a base to apex direction or in other words more nearly parallel to the line of Leads II and III as they make up their respective sides of the Einthoven triangle* Sinus tachycardia usually is the result of a reduction in vagal tone It is of course seen most commonly with fever shock hemorrhage thyrotoxicosis excitement and nervous disorders after exercise and in many toxic states It can be produced by such drugs as atropine which tends to paralyze the vagus or by amyl nitrite which reflexly diminishes vagal tone This disturbance usually begins and ends gradually in contrast to the other types of tachycardia in which the change is abrupt Carotid sinus stimulation usually reduces the rate gradually although in some patients it may produce transient atrioventricular block and in others it may have no appreciable effect This latter response is seen usually in patients who are seriously ill and in whom the rapid rate seems to be uninfluenced by any physiological stimuli An example of sinus tachycardia observed in a young woman with thyrotoxicosis is shown in Fig 4(a)

A rather distinct group of patients sometimes classified as having a *tendency to tachycardia* are those who have an abnormal response to

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[Whenever the wave of activation moves in a direction parallel to the line of a given lead the deflection produced in that lead will be large whenever the activation wave moves in a direction perpendicular to the line of a given lead the resultant deflection will be small]

falls during expiration It is almost universally found in children while in older individuals it may become perceptible on forced breathing In elderly patients the relation to the respiratory cycle may not be evident until the breathing is deepened whereafter the variations in the heart rate will tend to fall into step Sinus arrhythmia apparently is dependent upon variations in vagal tone It is most common when vagal tone is high as in

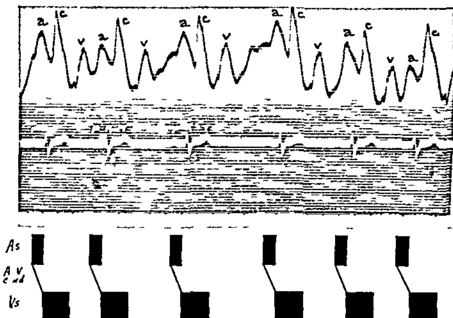


Fig 5 Sinus arrhythmia The upper tracing is a record of the venous pulse a auricular wave c and v ventricular waves The electrocardiogram is the middle record P auricular deflection R and S initial ventricular deflections T final ventricular deflection The cardiac mechanism is diagrammed below the electrocardiogram As auricular systole Vs ventricular systole A V cond a line representing the spread of the impulse through the junctional tissues. The interval between individual heart beats grows progressively longer and then shorter Except for this waning and waxing of the heart rate the cardiac mechanism is normal (From an article by F N Wilson [7])

athletes in individuals with slow heart rates and in patients receiving digitalis It tends to disappear when vagal tone is diminished as during exertion or emotion fever with amyl nitrite inhalation or after atropine Levine[10] has pointed out that when rheumatic fever occurs in a child the tendency to display sinus arrhythmia disappears and that as recovery occurs the arrhythmia reappears This arrhythmia has relatively little

This disorder is seen often for some weeks or months after acute infections such as influenza, but it occurs also in patients with effort syndrome [8] and in cases of anxiety neurosis. These patients usually have a basal heart rate below 100 per minute, and the abnormal response can be demonstrated by one of the simple exercise tests such as walking up and down a two step staircase twenty times. Although many of the causes of sinus tachycardia lie outside the heart, it is an important manifestation of acute cardiac disease as in acute rheumatic fever, acute myocardial infarction or acute pericarditis. It is a helpful sign in this group of disorders for the disease process usually may be considered active so long as the sinus tachycardia is present.

Sinus Bradycardia

Sinus bradycardia is a disorder in which the sole abnormality is a rate of impulse formation in the sino auricular node which is less than 60 beats per minute. Abnormally slow heart rates of this nature are rather common but of relatively little clinical significance. It is important that they be differentiated from heart block or slow radial pulse rates due to bigeminy with premature beats which are not felt at the wrist. Sinus bradycardia usually is the result of increased vagal tone. It occurs commonly in trained athletes, and particularly slow heart rates have been observed in men who have participated in long sustained exercise such as rowing or long-distance running [9]. It is associated also with jaundice and lesions causing increased intracranial pressure and is frequent in elderly individuals with arteriosclerosis. Often it is accompanied by sinus arrhythmia. Except for the slow rate the electrocardiogram is normal in all respects. An example of sinus bradycardia detected during the routine examination of a young student with a transient gastrointestinal disturbance is shown in Fig 4(b). It can be seen that the tracing is of normal character except for the slow heart rate.

Sinus Arrhythmia

Sinus arrhythmia is a disturbance of cardiac rhythm resulting from the irregular formation of impulses in the sino auricular node. It is a periodic waxing and waning of the heart rate which usually is closely related to the respiratory cycle, the heart rate rises with inspiration and

falls during expiration It is almost universally found in children while in older individuals it may become perceptible on forced breathing In elderly patients the relation to the respiratory cycle may not be evident, until the breathing is deepened whereafter the variations in the heart rate will tend to fall into step Sinus arrhythmia apparently is dependent upon variations in vagal tone It is most common when vagal tone is high as in

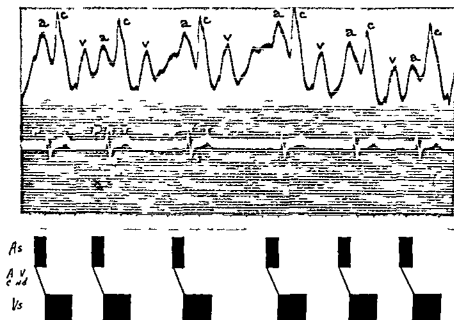


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clinical significance, but it must be distinguished from other, more important disorders of the cardiac rhythm It disappears on exercise whereas the rhythm in auricular fibrillation usually grows more chaotic after exertion The variations may be quite abrupt but the relation to the respiratory cycle is helpful in distinguishing sinus arrhythmia from partial heart block or premature beats which also may give rise to such sudden changes

Except for the cyclic variation in heart rate, the electrocardiogram in sinus arrhythmia is not altered Some cyclic variation in the outline of the P waves may be seen occasionally This is considered due to a change in the location of the pacemaker within the sino auricular node and is known as wandering or shifting of the pacemaker As the rate decreases the pacemaker is forced down to a lower level in the node and the spread of the impulse over the auricle is more nearly perpendicular to the axes of Leads II and III with the result that the P waves tend to become smaller or flat in Lead II and inverted in Lead III As the rate rises the pacemaker shifts to the cephalic end of the sino auricular node and the auricles are activated in a direction more nearly parallel to the line of Leads II and III with resultant upright taller P waves in those leads An example of sinus arrhythmia is shown in Fig 5 Except for the gradual cyclic variation in heart rate the electrocardiogram is normal in this patient as is the venous pulse tracing which was recorded simultaneously

Atrioventricular Nodal Rhythm

Of the specialized conduction tissues the atrioventricular node shows the quality of rhythmicity next in degree to the sino-auricular node If the activity of the latter is depressed or the activity of the former is enhanced the atrioventricular node may become the cardiac pacemaker, and the resultant rhythm is called an atrioventricular nodal rhythm Such a rhythm may be observed after many drugs such as digitalis adrenalin during acute infections or ether anaesthesia and upon exposure to atmospheres of low oxygen tension Wilson[31] has shown that it can be produced easily in normal individuals by vagal stimulation performed 10 to 15 minutes after hypodermic administration of atropine Not infrequently it is recognized first in electrocardiograms made in the course of general examinations in patients with no specific cardiac complaints Atrioventricular nodal rhythm has little clinical significance except that

it may draw attention to one of the situations cited above in which this disorder may appear It does not require any special therapy and although usually a transient phenomenon it may persist unchanged for some months or years

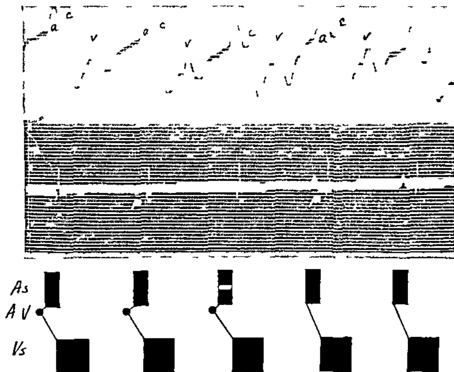


Fig 6 Atrioventricular nodal rhythm originating in the upper levels of the junctional tissues with transition to normal rhythm The upper record is the venous pulse tracing the middle record is the electrocardiogram and the lower chart is a diagram of the cardiac mechanism In the first two beats the a c and P R intervals are abnormally short and the P wave is inverted The fourth and fifth beats shown are normal In the third cycle the P wave is iso electric because two waves of excitation spread over the auricle one from the sino auricular node and the other from the atrioventricular node Since these two waves spread in opposite directions their electrical effect was to neutralize each other (From an article by F N Wilson [7])

The designation atrioventricular nodal rhythm is reserved properly for that type of disorder in which both the auricles and ventricles are responding to a pacemaker located in the atrioventricular node The

chief electrocardiographic features of this disorder are inverted P waves in Leads II and III with small or flattened P waves in Lead I and a shortened or reversed P-R interval The change in the form of the P waves is the result of the reversal of the normal direction of spread of activation over the auricle Since the interval between auricular and ventricular excitation (P-R interval) normally is largely a measure of the time required for the impulse to transverse the atrioventricular node, the location of the pacemaker within that structure alters the P R interval There are three general types of atrioventricular nodal rhythm depending upon the location of the pacemaker within the A V node (a) If it is high in the node the impulse arrives at the auricle before it reaches the ventricle, and the P R interval usually will range between 0 04 and 0 12 sec An example is shown in Fig 6 with a transition from atrioventricular nodal rhythm to sino-auricular nodal rhythm recorded (b) If the pacemaker is located in the central portion of the node, the impulse will arrive at the auricles and ventricles simultaneously with consequent superimposition of the P waves upon the QRS complexes Such P waves may be practically invisible and unless transitions are recorded or slight changes in the contour of the QRS complexes are detected, the cardiac mechanism may not be at once clear The diagnosis can be made oftentimes at the bedside in these patients because auricular and ventricular systole will be simultaneous, and there will be a large regurgitant pulse from the right auricle into the jugular veins An example is shown in Fig 7 and the contrast between the normal venous pulse and that with this type of atrioventricular nodal rhythm is easily seen in the phlebogram (c) Location of the pacemaker low in the atrioventricular node will result in activation of the auricles after the ventricles with the consequent appearance of the P wave after the QRS complex usually superimposed upon the RS-T segment with reversal of the P R interval or what is usually termed an R-P interval This type is shown in Fig 8 It is also associated with prominent jugular pulsations since auricular systole occurs during ventricular systole

Dissociation with Interference

An unusual type of atrioventricular nodal rhythm is that called auriculo ventricular dissociation with interference In this disorder the auricles are beating in response to the sino auricular node, but the ventricles are responding to a pacemaker in the atrioventricular node which

has a faster rate than that of the sinus node Furthermore there is a zone of unidirectional block which prevents the impulses from the atrioventricular node from passing back to the auricles The block is unidirectional because although the ventricular rhythm does not disturb that of the auricles from time to time there will occur what appear to be premature beats which actually represent impulses from the sinus node that have fallen in the interval when the A V node and ventricle are responsive and before the next atrioventricular nodal impulses can occur

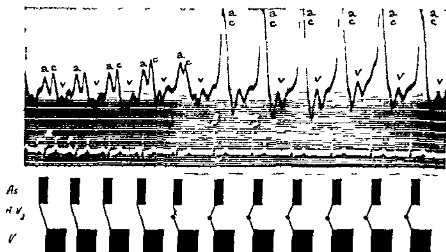


Fig 7 Atrioventricular nodal rhythm arising in the central zone of the junctional tissues The first four cycles are normal In the fifth cycle the auricles respond to the sino auricular node (the P wave is upright) but the ventricles respond to a center in the A V node In the final six beats both chambers respond to a center in the mid zone of the junctional tissues and the record shows no visible P wave because they are superimposed upon the QRS complexes The very tall a/c waves in the venous pulse are due to simultaneous auricular and ventricular systole This arrhythmia was produced in a normal subject by administration of atropine (From an article by F N Wilson ?)

This disorder of the cardiac mechanism is usually observed after toxic doses of digitalis or quinidine Wilson described one of the earliest cases recognized An example which occurred following large doses of quinidine used in the treatment of paroxysmal ventricular tachycardia is seen in Fig 8

Auricular Standstill

Auricular standstill is a rare disturbance of the cardiac mechanism in which there is no graphic evidence of auricular activity. This disorder has been observed usually during the administration of quinidine or digitalis or both; if it appears while these drugs are being given serious intoxication can be considered present and the medication should be discontinued without delay.[33] Patients with this phenomenon have displayed Adams-Stokes attacks, and it may be a premonitory manifestation of complete cardiac standstill. This disturbance was first recognized by Cushny as he made direct observations of animal hearts during administration of increasing doses of digitalis.[34] At toxic levels it was seen that the auricles ceased beating completely while the ventricles *continued to* beat slowly and regularly. The electrocardiogram displays no P waves

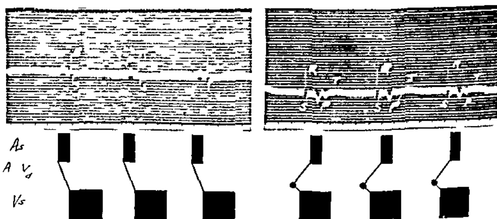


Fig. 8. The record on the left shows a normal cardiac mechanism. The record on the right illustrates atrioventricular nodal rhythm arising in the lower levels of the junctional tissues; the P waves are inverted and they occur after the QRS complexes producing an R-P interval. The diagram below illustrates that the pacemaker was so close to the ventricles that the impulse reached the ventricles before it could spread in a retrograde fashion to the auricles. This patient had mitral stenosis. (From an article by F. N. Wilson.[7])

at all, and usually there is a slow, regular ventricular rhythm maintained by an idioventricular pacemaker. This disorder can be confused easily with that type of atrioventricular nodal rhythm in which the P waves are lost in the QRS complexes. To be certain that the auricles are not beating, it may be necessary to make venous pulse tracings or to take

esophageal electrocardiograms As the patient recovers the gradual reappearance of the auricular deflections may be observed

Ventricular Escape

If unusual slowing of the normal sinus pacemaker occurs and the auriculoventricular node or auricular muscle fail to initiate an impulse single beats arising at levels below the junction of the A V node and His bundle may occur This phenomenon known as ventricular escape is seen usually during marked depression of the sino auricular node as during carotid sinus stimulation If the ventricular escape is initiated from a focus in the main stem of the His bundle the resultant QRS complex will be of normal outline If the escape arises from a site below the bifurcation of the His bundle it will be characterized by a slurred broad or notched QRS complex Ventricular escapes can be identified in the electrocardiogram by the slowing of the normal rhythm and the absence of P waves preceding the idioventricular beat

Disorders Due to Heart Block

Under certain abnormal conditions the passage of impulses from their origin in the sino auricular node to their destination in the ventricular myocardium may become partially or completely obstructed Such disturbances of the cardiac mechanism are classified as heart block If the blockade is complete a focus below the point of obstruction must become the cardiac pacemaker in order to sustain life The pathway for the impulse is so wide over much of its course particularly in the auricular and ventricular myocardium and the Purkinje network it is unlikely that solitary or even numerous scattered lesions in these locations will interfere with the conduction of the cardiac impulse The strategic situations are at those points where the path is narrow namely the atrioventricular node and the main stem of the His bundle localized areas of disease at these sites may easily impede or completely prevent passage of the wave of activation Lesions of the major branches of the His bundle also produce disturbances of conduction but these particular abnormalities produce such characteristic changes in the form of the electrocardiogram that they are better reserved for separate consideration under the heading of bundle branch block

Sino auricular Block

Sino auricular block is an uncommon disorder in which there is a complete dropping out of a single heart beat The electrocardiogram and venous pulse tracing show no evidence of either auricular or ventricular activity In addition, in order to make the electrocardiographic diagnosis of sino auricular block, the R-R interval enclosing the dropped beat must be exactly equal to two normal R-R intervals The example shown in Fig 9 displays these features very well and neither the venous pulse tracing nor the electrocardiogram display any evidence of cardiac activity during the long pauses This disorder is thought to be due to a barrier between the sino-auricular node and the auricular musculature which prevents the impulse from spreading out into the auricle as it does

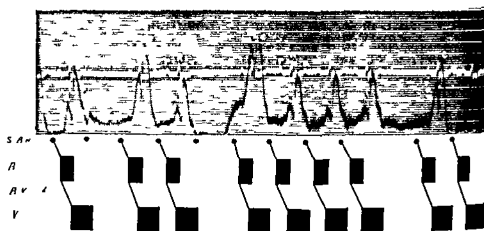


Fig 9 Sino auricular block At three points the rhythm of the auricles and ventricles is interrupted by pauses which are double the length of the normal cycle During these pauses there is no evidence of cardiac activity in either the electrocardiogram or in the record of the venous pulse It is supposed that the impulse fails to spread from the sino auricular node into the auricular muscle This arrhythmia was produced by administration of digitalis in a case of generalized arteriosclerosis (From an article by F N Wilson)

normally The muscular mass of the node in the mammalian heart is too small to give rise to a deflection in the electrocardiogram representing its activity so that this hypothesis is unproven Sino-auricular block is seen usually in patients receiving digitalis and under such circumstances it may be considered a sign of intoxication from that drug It may be confused at the bedside with occasional dropped beats due to partial

heart block or to blocked premature auricular beats It is less common than either of these disorders and electrocardiographic observations with special leads to record auricular deflections if necessary will show P waves in either of the latter two disorders Finally close observation of the neck veins often will reveal visible auricular pulsations at the time when the dropped beat occurs at the cardiac apex in partial heart block or with blocked premature auricular beats whereas they do not occur in *sino auricular block Sino-auricular block may be confused with marked* sinus arrhythmia but in the latter the long pauses do not appear abruptly they are of variable length and the record does not usually appear as if single complete cardiac cycles had dropped out This disorder usually requires no special therapy except that if it occurs during digitalis or quinidine therapy the drug should be discontinued until evidence of intoxication has cleared

Delayed Auriculo ventricular Conduction
(Prolonged P R Interval)

This disorder consists merely of a lengthening of the atrioventricular conduction time In adults a P R interval which is above 0 0-0 1 sec is considered abnormally long and Ashman and Hull[16] express the opinion that with rates above 100 an interval greater than 0 18 sec is *suggestive of disease The upper limit of normal may be considered for* practical purposes 0 14 0 16 in infants and 0 15 0 18 sec in older children Prolongation of the P R interval occurs in a wide variety of cardiac disorders but particularly in rheumatic fever in patients receiving digitalis and in individuals with chronic coronary arterial disease

Increase in the auriculoventricular conduction time is the most useful electrocardiographic change which accompanies acute rheumatic infection It occurs in a high percentage of the cases it may be considered evidence of rheumatic carditis and it is of some value as an index of degree of activity of the rheumatic process Most clinicians have had the experience of having a doubtful diagnosis of rheumatic fever confirmed by the discovery of a distinctly prolonged P R interval Usually as the disease subsides the P R interval shortens progressively The patient usually is considered to be in the active stage of the disease so long as the P R interval is changing from one observation to the next In some individuals the conduction time may remain prolonged even after the active stage of rheumatic fever has subsided probably because of scar

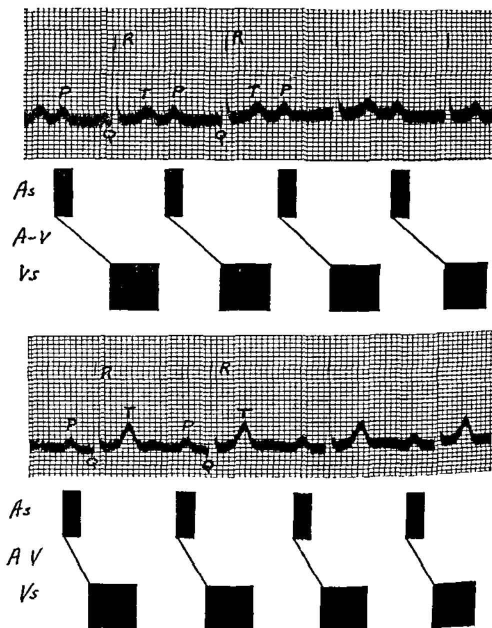


Fig 10 Prolongation of the P R interval In the upper record the P R interval measures 0 38 sec *This record* was made in a patient with an acute *infection* probably of rheumatic origin The lower record was made after the infection had subsided The P R interval measures 0 20 seconds the upper limit of the normal range (From an article by F N Wilson [7])

ring. An example of this disorder in an acute infection probably of rheumatic nature is shown in Fig. 10 with shortening of the conduction time to normal after the infection cleared.

When a long P-R interval is the result of digitalis, usually it is associated with U-shaped inversion of the T waves (Fig. 11). In this situation the lengthening is thought to be due in part to increased vagal tone and

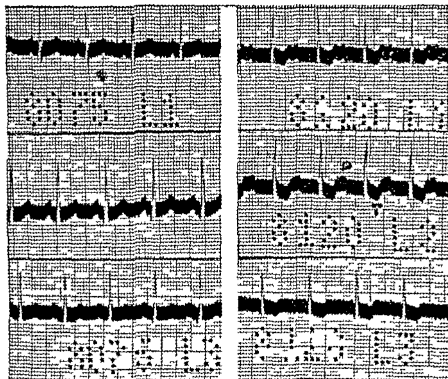


Fig. 11. Prolongation of the P-R interval produced by digitalis. Record 8073 was made before digitalis; the P-R interval measures 0.16 sec. Record 8 10 was taken after full doses of digitalis; the P-R interval measures 0.31 seconds. The characteristic U-shaped inversion of the T waves produced by digitalis is present in all leads. (From an article by F. N. Wilson in Cyclopedia of Medicine, F. A. Davis Co., Philadelphia.)

in part to the action of digitalis directly upon the specialized conduction tissue. This change in the electrocardiogram will clear in two or three weeks after stopping the drug if digitalis is responsible.

The only change seen in the electrocardiograms in this type of heart

block is the lengthened P-R interval Occasionally the P waves may be superimposed upon the T waves and must be looked for carefully The diagnosis may be suspected clinically particularly if there is a gallop *rhythm, and the intensity of the first heart sound at the apex is reduced* These changes occur because auricular systole is shifted back into the diastolic period If the heart rate is rapid the auricular and third heart sounds become superimposed, producing a summation type of gallop rhythm

Partial Auriculoventricular Block

As the activating impulse finds more and more difficulty in passing through the specialized tissues to the ventricles a point soon is reached at which an occasional impulse will fail to get through and a ventricular response will not occur This disturbance of cardiac rhythm is called partial heart block, and the missing ventricular contractions are known as dropped beats

When partial heart block is of low grade, only an occasional impulse fails to get through, and the dropped beats may occur quite irregularly In the electrocardiographic records of such patients the usual sequence is a progressive lengthening of the P-R interval up to the point where a beat drops out, as if the conduction tissue were becoming increasingly fatigued up to a point where the supraventricular impulse which is blocked meets a completely refractory junctional zone The first cycle after the dropped beat usually shows a much shorter P-R interval as if the long pause had permitted an opportunity for greater recovery with improvement in conductivity The progressive lengthening of the auriculoventricular conduction time usually does not occur at a uniform rate so that the increase in each interval is smaller than that in the preceding one Consequently as the P R interval grows increasingly longer the R R interval grows shorter, this gives rise to a quickening of the heart rate just before the dropped beat which can be detected clinically by careful auscultation This particular type of partial heart block often is referred to as the Wenckebach phenomenon and is produced usually by digitalis An example of this disorder is shown in Fig 12, and in this instance digitalis was responsible Occasionally low grade partial heart block will occur in which there is no appreciable lengthening of the P-R intervals preceding the blocked beats In such cases the ventricular pause in which the dropped beat falls will be equal to twice the normal R-R interval

As partial heart block increases in degree the tendency is for the block to occur regularly so that the ventricle may fail to respond to every fifth fourth third or second impulse thereby giving rise to 5 4 4 3 3 2 or 2 1 block (Fig 13) Regular 2 1 3 2 or 4 3 block are common whereas 3 1 or 4 1 block are infrequent Very often the block is variable from time to time leading to a quite complicated arrhythmia which is clear only from the study of graphic records

Partial heart block usually can be recognized correctly at the bedside if the clinician has an understanding of the nature of the disorder and the arrhythmias from which it must be differentiated When only an occasional beat is blocked the rhythm may resemble that of occasional premature beats In partial heart block the beat preceding the pause will be



Fig 12 Low grade partial heart block The fourth and ninth auricular contractions fail to produce ventricular responses Note that the dropped beats are preceded by progressive lengthening of the P R interval and by slight quickening of the ventricular rate This is known as the Wenckebach phenomenon This arrhythmia was produced by the administration of digitalis (From an article by F N Wilson[77])

of normal character and occur at the regular interval whereas an extra systole will be premature and often give rise to cardiac sounds of a different quality as well as developing a weaker radial pulse Auriculoventricular block of somewhat higher grade such as 2 1 block may be confused with sinus bradycardia or complete heart block Observation of the effects of reduction of vagal tone by means of exercise or the use of amyl nitrite or atropine may be helpful in such situations Diminution of vagal tone in sinus bradycardia causes a gradual increase in the heart rate with a gradual return to normal when the stimulus is removed In complete heart block the ventricular rate will be changed only very slightly or not at all although observation of the jugular veins may show a marked increase in the auricular rate Abrupt changes in the heart rate are commonly produced in partial heart block by diminishing vagal tone

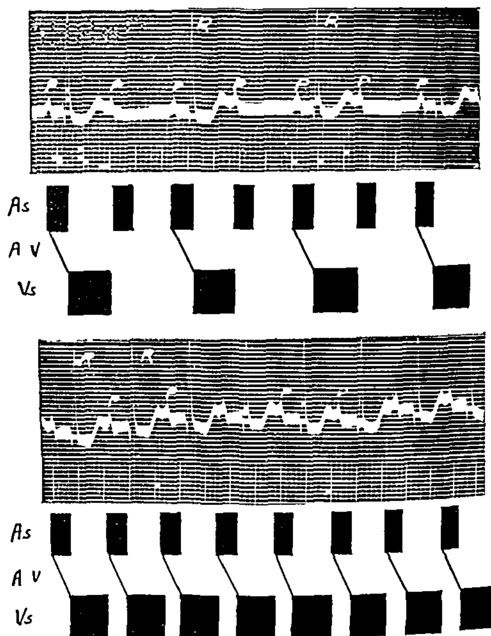


FIG 13 2 1 partial heart block In the upper record the ventricles respond to every other auricular contraction The block resulted from administration of digitalis The lower record was made to show the effect of amyl nitrite inhalation upon the partial heart block The ventricles are responding to every auricular impulse but the P R interval is slightly longer than normal (From an article by F N Wilson[7])

and in 2 1 heart block an almost exact doubling of the rate may occur (Fig 13) Such sudden striking changes in rate should suggest partial heart block *Extrasystolic bigeminy* must be distinguished from 3 2 auriculoventricular block in the former the interval between the normal beat and that preceding the long pause is brief and the extrasystole gives rise to a weaker radial pulse and usually to heart sounds of other than normal quality in the latter the interval between the two beats which precede the pause is nearly equal to one half the length of the pause and the corresponding heart sounds and pulses of the two beats are alike

The treatment of partial heart block depends upon the circumstances in which it occurs If it appears during digitalis therapy the drug should be discontinued temporarily and then begun again in smaller doses after the block has cleared Partial heart block usually is a transient phenomenon when it occurs during rheumatic fever or after an acute myocardial infarction Altschule and Blumgart have expressed the belief that heart block of this type should not contraindicate the use of digitalis if the usual indications are present

Complete Auriculoventricular Block

Complete auriculoventricular heart block develops when conductivity of the junctional tissues is reduced to such a level that auricular impulses are no longer able to pass through to the ventricles In order to maintain the circulation the potential pacemakers in the lower portion of the atrioventricular node the His bundle or its branches (depending on the location of the block) set up a slow regular independent rhythm with a rate which usually is 30 to 40 beats per minute The auricles *continue to beat at their usual rate in response to the sino-auricular node* although occasionally they may display some arrhythmia such as auricular fibrillation or flutter Complete heart block is most commonly the result of myocardial changes which are on an arteriosclerotic basis When this is the case the heart block is important in that it points to the underlying disease The higher degrees of heart block suggest that not only are the conduction pathways involved but in all probability other regions of the myocardium are diseased similarly If the lesions of acute rheumatic myocarditis acute myocardial infarction or syphilitic myocarditis develop in a strategic location interruption of the conduction pathways may occur with production of complete heart block Interventricular septal defects occasionally involve the His bundle and pro

duce this type of block Examples of congenital complete heart block without demonstrable structural anomalies have been observed The aortic valve and its supporting ring lie so close to the His bundle that calcification of those structures occasionally may produce this disorder Complete A-V block may appear in the course of diphtheria, under such circumstances it usually points to extensive myocardial involvement and is a grave prognostic sign

The electrocardiograms in patients with complete heart block display several distinctive features (Fig 14) The ventricular rhythm is perfectly regular and abnormally slow, *30 to 40 beats* per minute The auricles and ventricles beat independently and therefore the relationship of the P waves to the QRS complexes is variable from beat to beat The

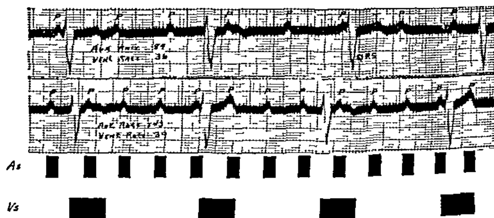


Fig 14 Complete heart block The upper record was made with the patient at rest *The lower record was made immediately after exercise Exertion increased the* auricular rate from 89 to 143 beats per minute but it produced almost no change in the ventricular rate The auricular and ventricular rhythms are completely independent of each other and the ventricular rate is unusually slow The QRS complexes are abnormal in outline This patient had syphilis (From an article by F N Wilson [7])

auricles are still under the control of the sino auricular node and consequently show an increase in rate in response to exercise or atropine or other measures which reduce vagal tone, since the conduction pathway is broken these measures usually do not affect the ventricular rate appreciably (Fig 14) There are rare exceptions usually in those patients with congenital complete heart block The configuration of the QRS complex in this disorder depends upon the site of the lesion and the location of the pacemaker The ventricular complexes will be normal in outline if the block is high in the atrioventricular node or in the main

stem of the His bundle, so that the pacemaker may be located low in the atrioventricular node or in the lower portions of the His bundle If the lesion is in the lower portion of the His bundle or in the bundle branches the pacemaker may be in one of the bundle branches and the QRS complexes will be abnormal in form The electrocardiographic diagnosis of complete heart block should include a statement that the ventricular complexes are normal or abnormal in outline However in the presence of abnormal complexes the additional diagnosis of bundle branch block cannot be made since it is not possible to tell whether the impulse arises above the bifurcation of the His bundle and has an abnormal spread over the heart or whether the pacemaker is located in one of the bundle branches and thereby gives rise to ventricular complexes of abnormal outline In some cases of complete heart block it will be found that the P P intervals which enclose a ventricular response are shorter than those in which ventricular systole does not occur This type of auricular arrhythmia usually is considered due to variations in vagal tone accompanying each ventricular systole

Complete heart block usually is recognized easily at the bedside It should always be considered when a patient presents a slow regular heart rate which is uninfluenced by exercise Careful auscultation usually discloses auricular sounds along the lower left sternal margin and medial to the cardiac apex Perhaps the most helpful auscultatory sign is that of variation in the intensity and quality of the first heart sound at the apex produced by the changing relations of auricular and ventricular systole The pulse pressure usually is high 80 1 0 mm Hg because of the slow heart rate and large cardiac output per beat Careful observation of the venous pulse in the neck may disclose auricular waves occurring at a different and faster rate than the cardiac apex beat

Syncopal attacks of Adams-Stokes type are seen commonly in patients with complete heart block These attacks result from ventricular standstill which may occur in several situations chiefly (a) when there is a change from normal rhythm to complete heart block (Fig 15) (b) when there is a change from partial to complete heart block (c) when ventricular activity suddenly ceases during a period of slow idioventricular rhythm (d) when the ventricular rate slows to an extremely low level or (e) when transitory ventricular tachycardia or ventricular fibrillation replaces the idioventricular rhythm[35] If the period of ventricular standstill is longer than four or five minutes death usually results from anoxia of the vital centers

The *treatment* of a patient with complete heart block must be

directed toward the underlying disease Once the cardiac disorder has become well established, many patients are able to perform a nearly normal measure of activity without much difficulty Special treatment is required only if Adams Stokes attacks are occurring, in such instances the sympathomimetic drugs, epinephrine, ephedrine, paredrine and racemic amphetamine sulfate are useful Metrazol, barium chloride atropine and desiccated thyroid are other measures which may be of value



FIG 15 Onset of complete heart block and an Adams Stokes attack The first four beats show no disturbance of conduction The last four auricular contractions are not followed by ventricular responses The period of ventricular standstill lasted many seconds the patient became unconscious and had a convulsion This patient had aortic valvular disease of undetermined etiology he died suddenly later while at the table presumably in a similar attack (From an article by F N Wilson[7])

DISORDERS OF HEART BEAT DUE TO ABNORMAL IMPULSE FORMATION

Not only does the heart generate regular rhythmic impulses in the specialized tissues but under certain conditions it produces impulses of another type which demonstrate certain distinctive features and apparently may arise anywhere in the heart The normal rhythmic impulses are said to give rise to homogenetic rhythms whereas the abnormal impulses in question initiate heterogenetic or ectopic rhythms Wilson has made a careful comparison of these two types of cardiac rhythms He has shown that homogenetic impulses have the following characteristics (1) they are formed in regular succession, each beat is one of a rhythmic series which may continue indefinitely, (2) each impulse is built up during a comparatively long pause after its predecessor, (3) they do not arise outside the specialized tissues, (4) their frequency is under the control of the extrinsic cardiac nerves (5) they ordinarily occur at low frequencies and (6) each impulse is independent of the

preceding one In contrast to these features are those of the heterogenetic impulses (1) they are usually isolated the process responsible for them being an intermittent one they therefore occur suddenly and even if they occur in series their cessation is abrupt (2) they appear to be discharged abruptly without a period of preparation (3) they may arise in all parts of the heart muscle (4) their frequency is not controlled by the extrinsic cardiac nerves (5) they occur at a high frequency when appearing serially and (6) each heterogenetic beat seems to bear some relation to the beat which precedes it When isolated heterogenetic impulses occur they give rise to premature beats or extrasystoles Serial heterogenetic impulses are responsible for the paroxysmal tachycardias In either case the disorder is further designated according to that part of the heart in which it is arising that is in the auricular or ventricular muscle or in the junctional tissues Heterogenetic impulses which arise outside the normal specialized tissues are sometimes called ectopic beats but not all heterogenetic rhythms are ectopic since they may sometimes arise in the specialized structures

Extrasystolic Arrhythmia

Isolated heterogenetic impulses give rise to premature beats or extrasystoles Such premature beats are labelled auricular nodal or ventricular depending upon the location of the focus from which they arise Premature beats occur nearly as often in people with otherwise normal hearts as in patients with significant heart disease They are not of themselves evidence of cardiac disease although when they occur a careful cardiac examination should be made Extrasystoles occur in all forms of heart disease but they may be somewhat more frequent in rheumatic valvular disease Some observers are of the opinion that frequent auricular premature beats are the forerunner of auricular fibrillation in patients with mitral stenosis In some instances extrasystoles seem to result from fatigue excessive smoking or overindulgence in caffeine containing beverages or alcohol In others minor infections or drugs such as epinephrine ephedrine or racemic amphetamine sulfate seem to be the precipitating factor Changes in posture or voluntarily altering the respiratory cycle may induce this arrhythmia occasionally It is usually abolished by exercise but in some individuals it appears only after exertion[37]

The sensations produced by extrasystoles are variable and in addi

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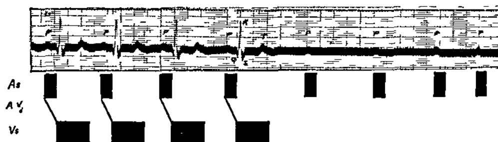


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electrocardiograms show certain distinctive features (Fig 16) (1) the premature beat appears before the next sequential beat would have occurred (2) definite premature P waves can be seen although they may be inconspicuous in one or two of the standard leads or if super imposed upon the T wave of the preceding normal beat may be indicated by only a notching or sharp peaking of that deflection (3) the outline

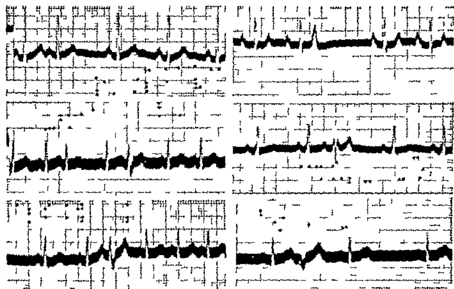


Fig 17 Auricular extrasystoles with aberrant ventricular responses No 26821 the third cycle is an auricular extrasystole the premature P deflection deforms the T wave of the second normal cycle The ventricular response to this premature auricular impulse differs in outline from the normal beats The QRS interval is 0 1 sec in duration and there is a broad slurred S wave This suggests that the spread of the premature impulse over the ventricle was abnormal and, in this case delay in activation of the right ventricle Similar aberrant responses to auricular extrasystoles are seen in No 24366 fifth cycle No 21071 lead III third cycle and No 11023 second cycle

Blocked auricular premature beat In the unnumbered record the T wave of the second cycle is very tall and peaked unlike the other T waves shown This result from a superimposed premature P deflection The long pause following this peculiar deflection indicates that the premature auricular impulse failed to traverse the junctional tissues or else met a refractory ventricle

of the premature P waves usually is different from that of the normal beats depending upon the location of the abnormal focus it will be nearly normal if the impulse arises in or near the sino-auricular node or it will be inverted in leads II and III if the focus is near the atrio

tion, there are pronounced individual differences in sensitivity to these sensations. Frequent premature beats, even if associated with significant heart disease, may produce no symptoms at all in some patients, whereas infrequent extrasystoles may cause great concern and even invalidism in others. Patients usually are more conscious of the disorder when quiet

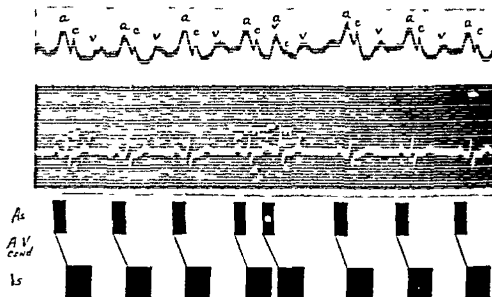


Fig. 16. Auricular premature beat. The fifth cycle is premature; the premature P deflection is superimposed upon the T wave of the preceding cycle and alters that deflection slightly. The QRS complex of the premature beat is identical with those of the normal beats. In the simultaneous venous pulse record the premature auricular contraction a falls upon the v wave of the preceding beat. (From an article by F. N. Wilson.)

or just after retiring than when they are active or working. Generally the patient complains of a "skipping" or "thumping" of the heart or a sensation that the heart has "turned over," "taken a flip-flop" or "dropped out of the chest." Occasionally there may be a transient sensation of choking, giddiness or precordial pain. The work of Kline and Bidder suggests that the patient usually is aware of the extrasystole itself, although some individuals may be aware of the extrasystolic pause or the next forceful, normal response which follows the extrasystole.

Auricular premature beats result from isolated, heterogenetic impulses arising in the auricles or sino-auricular node. The auricles beat prematurely, and the ventricles usually respond to this premature impulse. The

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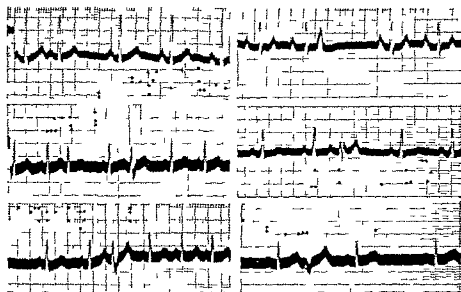


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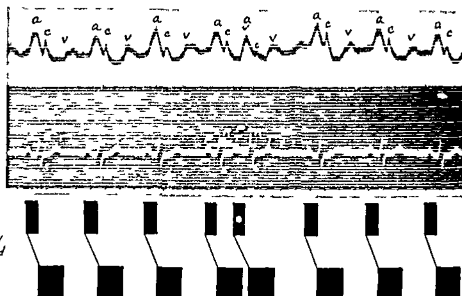


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disturb the normal auricular rhythm They are usually called *His bundle extrasystoles*

Ventricular premature beats display the following characteristics (Fig 19) (1) the ventricular complex is quite different in its configuration from the normal beats in that usually it is abnormally broad with large oppositely directed QRS and T deflections ( ) there are no

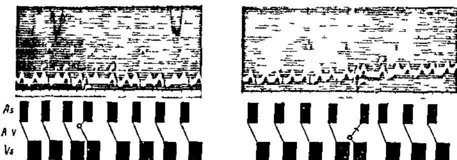


Fig 18 Atrioventricular nodal extrasystoles In the record on the left the fourth beat is premature The P wave is inverted the P R interval is unusually short and the QRS complex is identical with that of the normal beats This extrasystole arose in the upper level of the junctional tissues In the record on the right the fifth beat is premature The P wave is inverted but in this case it is superimposed upon the RS T segment of the premature complex The ventricular response to this premature beat was aberrant The extrasystole arose in the lower levels of the junctional tissues and spread to the ventricle before it reached the auricle (From an article by F N Wilson [7])

preceding P waves (3) the auricular rhythm usually is undisturbed because the heterogenetic impulses arising in the ventricle are not transmitted in a retrograde manner to reach and discharge the sino auricular node (4) because the ventricular muscle is still in a refractory state from the extrasystole the ventricle does not respond to the next auricular impulse which occurs after the premature beat (5) the pause following the premature beat is therefore fully compensatory The ventricular complexes of premature beats of this type differ from those of beats of supraventricular origin because the spread of the wave of activation over the ventricular myocardium is abnormal that is to say the order of stimulation is not the usual one since that portion of the heart in which the ectopic focus is situated will be activated first and that part of the heart which is most distant from this focus will be stimulated last As a matter of fact the site of origin of ventricular extrasystoles can be

ventricular node, (4) the P R interval of the premature beat is normal or slightly prolonged, (5) the ventricular complex has the same outline as the normal sequential beats except in those instances when the auricular impulse is so premature that the ventricular muscle is only partially recovered and the spread of the impulse over the ventricle is abnormal in that case the result will be so called aberrant ventricular responses which are to be differentiated from ventricular premature beats by the very fact that they are preceded by premature auricular impulses (Fig 17), (6) the pause, which follows an auricular premature beat is not fully compensatory that is to say the sum of the length of the cardiac cycle preceding the premature beat plus the length of the cycle to the next sequential beat usually is less than the sum of two normal cycles This is true because the ectopic auricular impulse discharges the impulse which was forming in the sino-auricular node, and the next impulse can then be developed there earlier than would have been the case, had there been no premature beat, (7) occasionally premature auricular beats may be blocked (Fig 17) This phenomenon will occur when the premature auricular impulse is unable to pass through the specialized conduction tissues to reach the ventricles (8) occasionally the extrasystolic impulse may disturb or depress the sino auricular node to such a degree that the pause after the extrasystole becomes longer than the normal R-R interval or the following beat may arise in the auriculoventricular node This latter phenomenon is called *dislocation of the pacemaker*

Premature beats which arise in the atrioventricular node usually are called *nodal* or *junctional extrasystoles* (Fig 18) In this disorder the P waves occur just before within or just after the QRS complexes depending upon whether the abnormal focus is high in the center or low in the A-V node just as is true in atrioventricular nodal rhythm The P-R interval is 0 12 sec or less or there is an R-P interval if the focus is low in the A-V node The P waves are inconspicuous or flat in lead I and inverted in leads II and III The ventricular complexes usually have the same outline as the normal sequential beats although they may be slightly modified by superimposed P waves, if the focus is in the middle of the A-V node Just as in the case of auricular extrasystoles the configuration of the QRS complexes will be aberrant if the ventricular conduction system has recovered incompletely from the preceding beat when the premature impulse reaches it There are in addition, extrasystoles of a rare form which arise in the junctional tissues but do not spread to the auricles Extrasystoles of this type display normal ventricular complexes a fully compensatory pause and do not

Extrasystoles may tend to appear with a definite regularity If every normal beat is followed by an extrasystole the result is bigeminy an example of this disorder is shown in Fig 20 Trigeminy appears when an extrasystole follows every two normal beats or if every normal beat

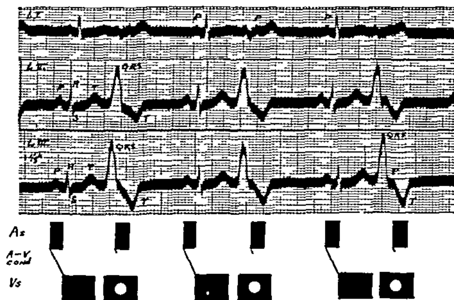


Fig 20 Bigeminy due to ventricular premature beats In these records every second beat is a ventricular extrasystole The normal P deflections which are superimposed upon the extrasystoles are indicated in Lead I and III This arrhythmia is commonly an indication of digitalis intoxication (From an article by F N Wilson)

is followed by two extrasystoles Quadrigeminy is the term applied when the disorder occurs in a sequence of four beats Although bigeminy and trigeminy may occur in any patient with extrasystoles they are commonly produced by digitalis particularly in patients with myocardial disease and auricular fibrillation and constitute one of the toxic manifestations of this drug Whenever these arrhythmias occur in patients receiving digitalis it is wise to evaluate the situation carefully and usually to discontinue the drug until the bigeminy disappears

Occasionally electrocardiograms are seen which display extrasystoles of varying outline (Fig 21) This indicates that the premature beats are arising from more than a single focus and suggests myocardial irritability of somewhat more than usual degree While this disturbance occurs

determined in most instances from the standard leads If the major deflection in lead I is positive (up) it is situated in the right ventricle whereas if it is negative (downward) the extrasystole can be said to

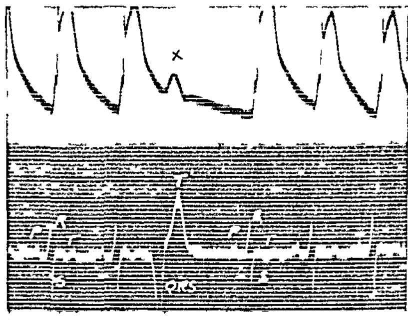


Fig 19 Ventricular premature beat The third cycle is premature The QRS complex is vastly different from the normal beats and it is not preceded by an auricular deflection The pause following the extrasystole is fully compensatory since the interval between the two beats enclosing the premature cycle is equal to twice the normal P R interval The ventricular extrasystole was so premature that it produced only a small impulse (X) in the carotid pulse recorded simultaneously (From an article by F N Wilson)

have arisen in the left ventricle Furthermore premature beats arising in the basal portions of the left ventricle produce upward deflections in leads II and III whereas those coming from points near the apex display downward or negative major deflections in leads II and III These points were made clear by the fundamental observations of Barker Macloed and Alexander when they produced extrasystoles by stimulating various points on the surface of an exposed human heart[3] From a functional point of view the origin of the extrasystolic impulse is unimportant the stroke output of the premature beat is determined by its degree of prematurity and the volume of blood within the heart when it contracts

may spread occasionally through the junctional tissues from below upward i e in exactly the reverse of the normal direction this produces an auricular response which follows the ventricular systole and also discharges any impulse forming in the sino auricular node (Fig -3) Because ventricular extrasystoles which are accompanied by retrograde activation of the auricles disturb the auricular rhythm the pause following the extrasystole usually falls short of being fully compensatory If the sino auricular node and the ectopic center within the ventricle discharge at nearly the same time the ventricular myocardium may respond

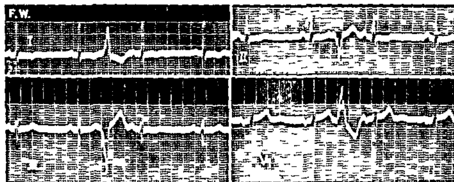


Fig 22 Interpolated ventricular extrasystoles In each record the third cycle is a ventricular premature beat interposed between two normal beats The extrasystoles are not followed by compensatory pauses The inverted T waves in lead I are abnormal and the T waves are slightly modified in all leads in the first post extrasystolic cycles The patient had hypertensive arteriosclerotic heart disease and was receiving digitalin

in part to the supraventricular impulse and in part to the extrasystolic focus This phenomenon is called interference and produces ventricular complexes which are transitional in form between the normal beats and those produced when the ventricle beats entirely in response to the heterogenetic focus

The clinical recognition of extrasystoles usually presents no great difficulty In the course of the examination attention may be drawn first to the intermittent pulse when the radial pulse is palpated or as the blood pressure is measured The pulse at the wrist may display weak premature beats followed by pauses of greater than normal length or if the extrasystole is so premature that it puts out very little blood or even so little that it fails to open the semi lunar valves there may be no impulse at all at the wrist The arrhythmia usually is easily apparent upon cardiac

rarely in normal people, it occurs frequently as a result of excessive digitalis and under such circumstances the drug should be stopped until the arrhythmia clears Isolated ventricular premature beats of constant form are not as clear-cut a sign of digitalis intoxication but if observation of the patient before and during digitalis therapy indicates that the extrasystoles first appeared after exhibition of the drug it should be continued only under very close supervision

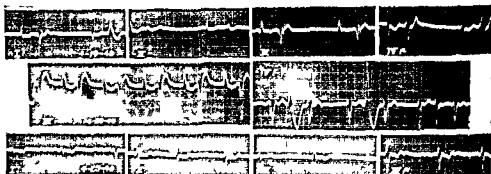


Fig 21 Ventricular extrasystoles arising from multiple foci April 19 1940 every second cycle is a ventricular premature beat In each lead the two extrasystoles shown are distinctly different in outline April 2 1940 Lead III shows ventricular tachycardia with bi directional QRS complexes lead IV shows ventricular extrasystoles (second fifth and eighth cycles) of varying form April 25 1940 auricular fibrillation This patient had rheumatic heart disease with aortic mitral and tricuspid valvular disease and severe digitalis intoxication (Observed by the author at the Peter Bent Brigham Hospital)

Ventricular extrasystoles usually are not extra beats, since they only replace a normal beat of supraventricular origin If the heterogenetic focus discharges late enough after the preceding beat so that it finds the ventricular muscle responsive and yet not too late in the diastolic period the extrasystolic cycle may be fully completed and the next normal impulse may also find the ventricle in the responsive rather than in the refractory state Such an extrasystole is truly an extra beat and is seen to be sandwiched in between two normal beats (Fig) Premature beats of this type are designated as *interpolated*, ventricular extrasystoles They are not followed by a compensatory pause but the P-R interval of the beat following the extrasystole commonly is of slightly more than normal length because the extrasystolic impulse renders the His bundle somewhat refractory to the succeeding supraventricular impulse

The wave of activation which originates ventricular premature beats

may spread occasionally through the junctional tissues from below upward, i.e., in exactly the reverse of the normal direction; this produces an auricular response which follows the ventricular systole and also discharges any impulse forming in the sino-auricular node (Fig. 23). Because ventricular extrasystoles which are accompanied by retrograde activation of the auricles disturb the auricular rhythm, the pause following the extrasystole usually falls short of being fully compensatory. If the sino-auricular node and the ectopic center within the ventricle discharge at nearly the same time, the ventricular myocardium may respond

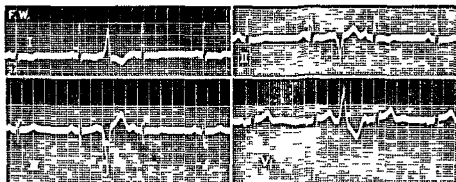


Fig. 22. Interpolated ventricular extrasystoles. In each record the third cycle is a ventricular premature beat interposed between two normal beats. The extrasystoles are not followed by compensatory pauses. The inverted T waves in lead I are abnormal, and the T waves are slightly modified in all leads in the first post-extrasystolic cycles. This patient had hypertensive arteriosclerotic heart disease and was receiving digitoxin.

in part to the supraventricular impulse and in part to the extrasystolic focus. This phenomenon is called interference and produces ventricular complexes which are transitional in form between the normal beats and those produced when the ventricle beats entirely in response to the heterogenetic focus.

The clinical recognition of extrasystoles usually presents no great difficulty. In the course of the examination attention may be drawn first to the intermittent pulse when the radial pulse is palpated or as the blood pressure is measured. The pulse at the wrist may display weak premature beats followed by pauses of greater than normal length, or if the extrasystole is so premature that it puts out very little blood or even so little that it fails to open the semilunar valves, there may be no impulse at all at the wrist. The arrhythmia usually is easily apparent upon cardiac

auscultation Ventricular extrasystoles often display cardiac sounds which are altered in quality and intensity, in that they are more faint than those of the normal beats or if the ventricular premature beat and normal auricular systole are simultaneous, the first heart sound at the

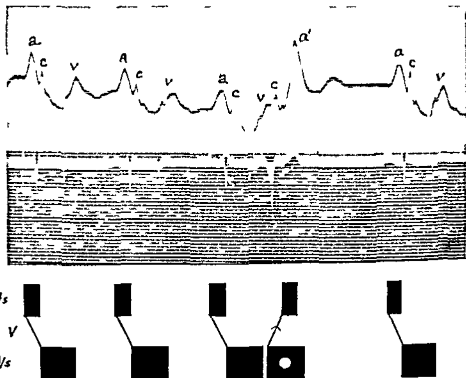


Fig 3 Ventricular premature beat with retrograde activation of the auricle The fourth cycle is a ventricular extrasystole The ventricular impulse spread through the junctional tissues in a retrograde fashion to produce an auricular response indicated by the inverted P wave superimposed upon the RS T segment of the extrasystolic complex Simultaneous auricular and ventricular systole produced the tall a wave in the venous pulse illustrated above Such ventricular extrasystoles usually are not followed by a fully compensatory pause (From an article by F N Wilson [7])

apex may be unusually loud On the other hand, if the sounds produced by the extrasystole are of much the same character as those of the normal beats the premature beats probably are of auricular origin The measurement of the length of the compensatory pause is often cited as another aid in the bedside differentiation of the origin of extrasystoles but this calls for rather precise timing and, as has been indicated, ventricular premature beats are not always followed by a fully compensatory pause

Interpolated ventricular premature beats usually can be diagnosed from the unusual peculiar succession of multiple heart sounds which they produce Extrasystoles are confused most often with auricular fibrillation and when they are numerous and arising from multiple foci graphic records may be the only means of distinguishing these two disorders Certain features are helpful (a) extrasystoles tend to be a transient phenomenon whereas auricular fibrillation is more apt to be permanent (b) any measure which tends to increase the heart rate also tends to abolish extrasystoles except in those rare instances in which exercise actually seems to produce them[3] whereas such procedures tend to make the arrhythmia more chaotic in the presence of auricular fibrillation (c) if long pauses occur which are always preceded by cycles of brief duration the arrhythmia usually is due to extrasystoles whereas long pauses preceded by beats of normal length suggest auricular fibrillation (d) extrasystoles usually do not occur with rapid heart rates When both extrasystoles and auricular fibrillation are present the electrocardiogram usually is the only means for distinguishing them The differentiation of extrasystoles and partial heart block has been discussed in an earlier section of the chapter

The *management of extrasystolic arrhythmia* depends on the circumstances in which it occurs If the patient is unaware of the disorder and no specific etiological factor is apparent it should be disregarded and in fact the patient s attention should not be directed to the disorder lest he become disturbed by it It may be well to try elimination programs to determine whether alcohol tobacco caffeine or other specific agents are responsible Reassurance to the patient that the premature beats cause no functional disturbance usually will set his mind at ease and may make him less aware of the disorder If the extrasystoles develop first after digitalis has been given or if extrasystolic bigeminy or extrasystoles arising from multiple foci appear in a patient receiving digitalis the drug should be discontinued at once Quinidine or papaverine may be effective in reducing the frequency of the extrasystoles but giving the patient some medication may nullify your reassurance to him that the arrhythmia is innocuous However in those patients who develop extrasystoles upon exertion quinidine often has great prophylactic value There is considerable justification for using quinidine in patients with a recent myocardial infarction who display ventricular extrasystoles in an effort to forestall more serious disturbances such as ventricular tachycardia or ventricular fibrillation Some clinicians are inclined to use quinidine prophylactically to prevent serious arrhythmias in patients with recent

myocardial infarction but since this drug is definitely a myocardial depressant and since small doses have been shown to produce disturbances of conduction in occasional individuals with normal hearts[40], the writer cannot subscribe to this as a routine practice

Paroxysmal Tachycardia

The term paroxysmal tachycardia is used to designate those types of paroxysmal rapid heart action which appear to consist of a rapid succession of premature beats There are two general classifications of this disorder divided according to the location of the abnormal pacemaker, (1) supraventricular tachycardia including auricular tachycardia, which is the most common form and atrioventricular nodal tachycardia which is the least common and (2) ventricular tachycardia which is less common but usually more serious than auricular tachycardia A special type of supraventricular tachycardia auricular tachycardia with atrioventricular block will be given separate consideration It is not within the scope of this presentation to discuss in detail the nature of the disturbance underlying paroxysmal tachycardia Although many have held the view that paroxysmal tachycardia is due to heterogenetic impulse formation, recent evidence has suggested that it may be related to the circus rhythms such as auricular flutter and fibrillation[41]

Paroxysmal tachycardia has many significant features which are peculiar to it The heart rate during the attack usually is 150 to 220 per minute although in children the rate may be as high as 300 to 350 The attacks may last from just 3 to 4 beats to periods of several days The frequency with which the paroxysms occur varies widely from one patient to another but as a rule the more frequently the attacks occur the shorter their duration tends to be Short attacks usually cause the patient no more difficulty than single isolated extrasystoles Although paroxysmal tachycardia tends to be more common in patients with other evidence of heart disease in some individuals it may constitute the sole cardiovascular abnormality The onset and offset of the attacks are abrupt the first beat of the paroxysm bearing a relation to the preceding normal rhythm just like that of a single extrasystole This sudden onset is quite unlike the gradual one which occurs with sinus tachycardia The cardiac rhythm during the paroxysm usually is very regular although auricular tachycardia is not always absolutely so[4] and ventricular tachycardia often is distinctly irregular[43] The various factors such as exertion

amyl nitrite and variations in breathing which influence the heart rate under most circumstances do not alter it appreciably when paroxysmal tachycardia is present except as these procedures may increase vagal tone to such a level as to stop the paroxysm if it is of supraventricular origin

The *symptoms* associated with paroxysmal tachycardia are dependent upon three major facts (1) the rapidity of the heart rate developed (2) the duration of the attack and (3) the condition of the patient s heart As a general rule the higher the rate the more severe the symptoms Similarly the longer the attack the greater is the likelihood that serious complications will occur Even when the heart is otherwise normal signs of cardiac failure may appear if paroxysmal tachycardia lasts for seven to ten days or more If the heart is abnormal as in mitral stenosis or coronary arterial disease signs of cardiac embarrassment will appear sooner In addition as in most diseases the patient s threshold for discomfort is an important factor Some patients are able to continue working despite the disturbance whereas others must take to their beds The usual symptoms at the onset of the attack are palpitation weakness or giddiness After about an hour many patients develop nausea and vomiting this sometimes may cause the attack to end Cardiac pain appears in some individuals probably those who have coronary arterial disease and latent angina pectoris with distress appearing when the tachycardia produces an inadequate coronary blood flow Another indication that circulation may be insufficient during paroxysmal tachycardia is persistent changes in the T waves which have been observed for several days or weeks after normal rhythm has been restored[11, 4] If the situation grows more serious either because of the long duration of the attack or because of associated heart disease the usual manifestations of congestive heart failure make their appearance Many patients report a thumping in the chest or throbbing in the head just at the onset or offset of the attacks These latter sensations probably are due to isolated extrasystoles

Paroxysmal tachycardia of supraventricular origin is so designated because the abnormal pacemaker is located above the bifurcation of the His bundle The ventricular complexes are therefore usually of normal outline and similar to those present during normal rhythm in the given case The electrocardiogram resembles a rapid succession of auricular of auriculoventricular nodal premature beats The subclassification of any case as auricular or nodal is usually difficult because the P waves are small or flat and they are nearly always superimposed upon and obscured by the T waves If the P waves can be defined and it is seen

that they are inverted in leads II and III together with a shortened or reversed P-R interval just as in auriculoventricular nodal extrasystoles the diagnosis of nodal tachycardia can be considered, but even then it is not always possible to ascertain to which cardiac cycle the P waves belong A record of the onset or offset of the paroxysm usually is very helpful in making a more exact diagnosis Abnormal ventricular complexes are not of themselves sufficient to differentiate supraventricular from ventricular tachycardia because abnormal QRS complexes and T waves may occur during supraventricular tachycardia in two situations (1) the ventricular responses may become aberrant due to the rapid rate and fatigue of the specialized tissues and the ventricular muscle and ( ) intraventricular block present during normal rhythm and giving rise to abnormal QRS and T deflections will also be present during any attack of paroxysmal tachycardia the patient may develop

The P R interval during *paroxysmal auricular tachycardia* usually is longer than during normal rhythm because of fatigue of the specialized conduction tissues This is well shown in the example illustrated in Fig -4 In this case the P R interval is so long that the P wave is superimposed upon the RS T segment and T wave of the preceding beat This together with the inversion of the P waves suggests atrioventricular nodal tachycardia but the absence of an inverted P wave following the last beat of the paroxysm excludes this diagnosis Because of the abnormal location of the auricular pacemaker the P waves are often inverted in auricular tachycardia If the P waves are submerged in the ventricular complexes in the standard leads occasionally they may be brought out to better advantage by special leading from the precordium along the right sternal margin[16] or from the esophagus at the auricular level[1] The heart rate during supraventricular tachycardia usually is 180 to 2-0 per minute Occasionally it may be more rapid particularly in children[18] and at times it may be much slower A case with multiple brief paroxysms with a rate of only 1 4 per minute is shown in Fig -5 The nature of the onset of the paroxysms just as isolated premature auricular beats and the mechanism of the offset of the attacks with simple abrupt cessation or at other times with blocked auricular impulses is particularly well shown in this series of tracings Supraventricular tachycardia can be differentiated from sinus tachycardia by the fact that the former begins and ends suddenly usually develops a more rapid rate can often be brought to an abrupt end by vagal stimulation and nearly always displays inconspicuous auricular deflections in the electrocardiograms On the other

hand sinus tachycardia begins and ends gradually rarely develops a rate faster than 140 to 160 except in young children displays P waves which are tall and almost always easily seen in the electrocardiograms and usually is slowed gradually and only temporarily by vagal stimulation The differentiation of supraventricular tachycardia from other types of paroxysmal rapid heart action will be taken up in the later discussions of the individual disorders

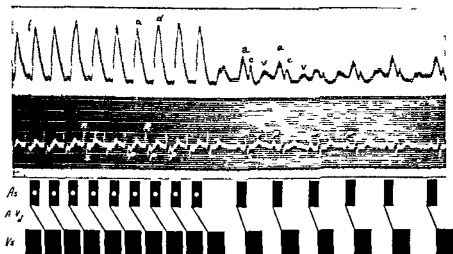


FIG 4 Paroxysmal auricular tachycardia The first ten cycles shown are the final portion of a paroxysmal tachycardia of auricular origin In this case during the attack the P waves are inverted and superimposed upon the RS T segment The last beat of the paroxysm is not followed by such a P deflection the possibility of atrioventricular nodal tachycardia thereby is excluded The QRS complexes during the paroxysm are identical with those during normal rhythm The large venous pulses during the paroxysm were due to the prolongation of the P R interval and consequent simultaneous auricular and ventricular systole (From an article by F N Wilson [7])

Although paroxysmal supraventricular tachycardia occurs commonly in patients with organic heart disease particularly mitral stenosis it is also frequently encountered in individuals who have no other evidence of cardiovascular disease It is seen quite frequently in patients with thyrotoxicosis and it may be the initial manifestation of masked hyperthyroidism [49] It may occur under any circumstances at work or at rest but in some persons it seems that assuming a certain position such as bending over to lace a shoe or turning abruptly to the left side may

that they are inverted in leads II and III together with a shortened or reversed P-R interval just as in auriculoventricular nodal extrasystoles the diagnosis of nodal tachycardia can be considered, but even then it is not always possible to ascertain to which cardiac cycle the P waves belong A record of the onset or offset of the paroxysm usually is very helpful in making a more exact diagnosis Abnormal ventricular complexes are not of themselves sufficient to differentiate supraventricular from ventricular tachycardia because abnormal QRS complexes and T waves may occur during supraventricular tachycardia in two situations, (1) the ventricular responses may become aberrant due to the rapid rate and fatigue of the specialized tissues and the ventricular muscle and (2) intraventricular block present during normal rhythm and giving rise to abnormal QRS and T deflections will also be present during any attack of paroxysmal tachycardia the patient may develop

The P-R interval during *paroxysmal auricular tachycardia* usually is longer than during normal rhythm because of fatigue of the specialized conduction tissues This is well shown in the example illustrated in Fig 24 In this case the P R interval is so long that the P wave is superimposed upon the RS T segment and T wave of the preceding beat This together with the inversion of the P waves suggests atrioventricular nodal tachycardia but the absence of an inverted P wave following the last beat of the paroxysm excludes this diagnosis Because of the abnormal location of the auricular pacemaker the P waves are often inverted in auricular tachycardia If the P waves are submerged in the ventricular complexes in the standard leads occasionally they may be brought out to better advantage by special leading from the precordium along the right sternal margin[46] or from the esophagus at the auricular level[4] The heart rate during supraventricular tachycardia usually is 180 to [illegible]0 per minute Occasionally it may be more rapid particularly in children[48], and at times it may be much slower A case with multiple brief paroxysms with a rate of only 124 per minute is shown in Fig 25 The nature of the onset of the paroxysms just as isolated premature auricular beats and the mechanism of the offset of the attacks with simple abrupt cessation or at other times with blocked auricular impulses is particularly well shown in this series of tracings Supraventricular tachycardia can be differentiated from sinus tachycardia by the fact that the former begins and ends suddenly, usually develops a more rapid rate, can often be brought to an abrupt end by vagal stimulation and nearly always displays inconspicuous auricular deflections in the electrocardiograms On the other

occurs It has been suggested that increase in reflex sympathetic action because of hypotension makes the more protracted paroxysms more difficult to stop, it may, therefore be quite advantageous to have the patient himself make efforts to stop the attack immediately after the onset If these simple measures are ineffective the drugs which may be used include syrup of ipecac (4 to 8 c c repeated after 20 to 30 minutes if necessary) digitalis (0 5 gm intravenously if none has been given previously) digitoxin (0 4 to 1 0 mgm orally or intravenously if none has been given previously) and mecholyl acetyl B methyl choline (10 to 40 mgm subcutaneously) If mecholyl is used atropine should be kept ready in a syringe to be given intravenously in doses of 1 to mgm as an antidote for the severe collapsing reactions which sometimes occur Many patients find that if they lie down and fall asleep the heart action will have been restored to normal when they awaken Barbiturates or opiates may be used to induce such a period of rest frequently with quite satisfying results

Paroxysmal ventricular tachycardia resembles a rapid succession of ventricular extrasystoles The ventricular rate usually is 160 to 210 per minute The pacemaker is located below the bifurcation of the His bundle the spread of the impulse is abnormal and the ventricular complexes are therefore of abnormal outline and quite unlike those present during normal rhythm However as has been pointed out the abnormal form of the QRS and T deflections during the period of rapid heart action does not by itself permit the diagnosis of paroxysmal ventricular tachycardia That conclusion may be reached with certainty only when the nature of the auricular activity is clear otherwise there may be confusion with cases of supraventricular tachycardia with aberrant ventricular responses or supraventricular tachycardia occurring in a person, who has a defect in intraventricular conduction even with a normal rate In many cases of ventricular tachycardia the auricles continue to beat at a normal independent rate or at least at a rate different from that developed by the ventricles In other cases there may be associated auricular fibrillation auricular flutter or auricular standstill Occasionally the ectopic impulses are conducted in a retrograde fashion so that the auricles respond to each of the ventricular impulses or to a certain fraction of them It is often necessary to look for other electrocardiographic evidence to support the diagnosis This may consist of isolated ventricular premature beats having the same outline as the QRS complexes recorded during the tachycardia or a record of the onset of the attack just as a ventricular extrasystole or tachycardia of ventricular

bring on an attack The use of alcohol, tobacco or caffeine containing beverages seems to precipitate the attacks in some cases and if this is the case the elimination of the offending agent may bring the paroxysms to an end In other patients the attacks occur during periods of chronic fatigue exhaustion or in association with infections If the attacks recur frequently, the judicious use of quinidine or digitalis may give gratifying prophylactic effects It does not seem worthwhile to give these drugs for long periods if the attacks occur infrequently

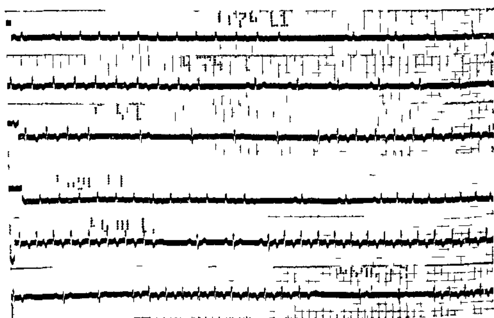


FIG , Paroxysmal auricular tachycardia Numerous paroxysms of brief duration are shown All of the onsets and offsets are abrupt The first beat of the paroxysm bears the same relation to the preceding normal beat as would an isolated auricular premature beat Some offsets occur because of failure of the ventricle to respond as in No 4650 leads II and III other paroxysms stop because the auricular tachycardia ceases as in No 46 4 leads II and III

Paroxysmal supraventricular tachycardia usually responds to the simple measures which increase vagal tone These include forced maintained inspiration deep inspiration and straining against a closed glottis induced gagging ocular pressure and carotid sinus stimulation The last of these usually is the most effective and patients can often be taught to locate and massage one or the other of the carotid sinuses when an attack

without a post paroxysmal pause can be seen also in this illustration An example of paroxysmal ventricular tachycardia with 1 1 retrograde stimulation of the auricles is seen in Fig 7 Inverted P waves can be

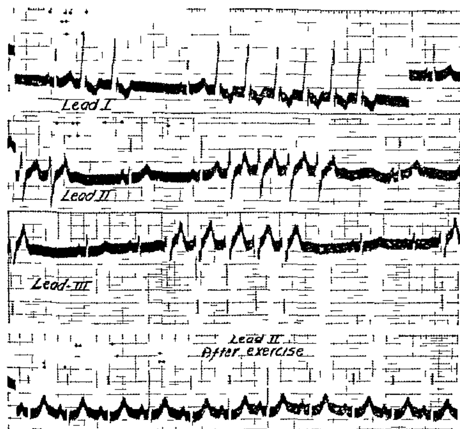


Fig 27 Paroxysmal ventricular tachycardia with 1 1 retrograde auricular activation Brief paroxysms are shown in the upper three records In each lead but most marked in lead II the T waves during the paroxysm are deformed by inverted P waves indicating that the ventricular impulse had spread through the junctional tissues to activate the auricle from below The arrhythmia was abolished by exercise This patient was a twelve year old boy who had no other evidence of heart disease (From an article by Rosenbaum and associates [6])

seen superimposed upon the ascending limb of the T waves particularly in lead II The observations illustrated in this figure were made in a 1 year old boy who had no evidence of structural heart disease and

form occurring in the presence of known long-standing auricular fibrillation. If the offset of the paroxysm is recorded and there is no postparoxysmal pause before normal rhythm begins, this sequence means that the disorder was of ventricular origin, that the auricles were beating independently, and that the sino-auricular node was ready to resume its function as the pacemaker immediately. The presence of a postparoxysmal pause is not helpful, however, since such a sequence may occur in either ventricular or supraventricular tachycardia.

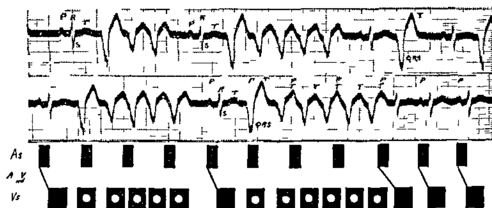


Fig. 6. Paroxysmal ventricular tachycardia. The paroxysms consist of three to six ventricular extrasystoles in succession and illustrate the onset and offset of this arrhythmia. The first one or two beats of each paroxysm show minor differences in configuration from the succeeding cycles. The auricular rhythm is undisturbed by the tachycardia and superimposed P waves can be discerned. This patient had attacks in variably induced by exertion. He later died suddenly a few minutes after the onset of an attack. (From an article by F. N. Wilson.)

Several of the electrocardiographic features of paroxysmal ventricular tachycardia are well shown in Fig. 6. The abnormal form of the ventricular complexes during the tachycardia as contrasted with the configuration of the normal beats is well demonstrated. Not only does the first beat of the paroxysm resemble a ventricular extrasystole, but it can be seen that the first few beats of each sequence are always very similar in form and slightly different from the later beats, as if the attack always began in the same manner and required a few beats before settling into a certain definite pathway. Isolated extrasystoles having the same form as the beats of the paroxysm, the lack of disturbance of the auricular rhythm and cessation of an attack with resumption of normal rhythm

without a post paroxysmal pause can be seen also in this illustration An example of paroxysmal ventricular tachycardia with 1 1 retrograde stimulation of the auricles is seen in Fig 27 Inverted P waves can be

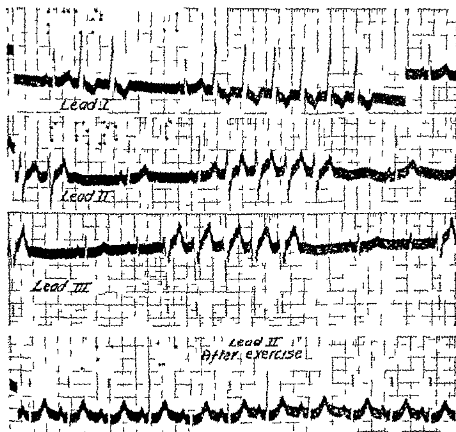


Fig 27 Paroxysmal ventricular tachycardia with 1 1 retrograde auricular activation Brief paroxysms are shown in the upper three records In each lead but most marked in lead II the T waves during the paroxysm are deformed by inverted P waves indicating that the ventricular impulse had spread through the junctional tissues to activate the auricle from below The arrhythmia was abolished by exercise This patient was a twelve year old boy who had no other evidence of heart disease (From an article by Rosenbaum and associates)

seen superimposed upon the ascending limb of the T waves particularly in lead II The observations illustrated in this figure were made in a 1 year old boy who had no evidence of structural heart disease and

who had frequent, brief symptomless paroxysms of ventricular tachycardia

Paroxysmal ventricular tachycardia may be associated with almost any type of heart disease, and although it may occur in the absence of other evidence of cardiac abnormalities this is less often the case than in supraventricular tachycardia Ventricular tachycardia occurs commonly as a complication of acute myocardial infarction [9] In such a situation it is most important that the disorder be recognized and properly treated because a heart with a fresh infarct is in no condition to withstand an extremely rapid heart rate or the insufficient coronary blood flow which accompanies it This disorder may result also from excessive digitalis[51] In many of the examples produced by digitalis electrical alternans or so-called bi directional ventricular tachycardia may be observed (Fig 21), this consists of alternation of the chief deflections of the QRS complexes from beat to beat[5, 53] Digitalis therapy should be discontinued immediately in such a situation The various situations, in which ventricular tachycardia may appear have been discussed in the reviews of Cooke and White [1] and Williams and Ellis This disorder may occur also in childhood and may complicate congenital heart disease

There are certain *clinical observations* which may be helpful in distinguishing ventricular tachycardia from other forms of paroxysmal rapid heart action The irregularity of the ventricular rate may be such that variations in the length of the successive heart cycles can be detected by auscultation Frequently due to changing relations between auricular and ventricular systole there are variations in the quality and intensity of the first heart sound at the apex much as in complete heart block This sign will be present in those subjects whose auricles are beating regularly and independently Patients of this type may display also a visible jugular pulse with a rate slower than the apical heart rate Finally the various techniques of vagal stimulation which frequently cause supraventricular tachycardia to stop abruptly have no effect whatever on tachycardia arising in the ventricles

The need for differentiating supraventricular from ventricular tachycardia rests in the fact that the measures usually used in the treatment of the former are ineffective in the latter As a matter of fact some of the drugs such as digitalis may make the patient with ventricular tachycardia worse Quinidine is the drug of choice in the treatment of this disorder No definite rules can be given regarding dosage, but it is well to remember that the excretion time is relatively rapid and to be successful it may be necessary to give doses of increasing size at frequent regular

intervals A single dose of 0.2 gm may suffice in some cases whereas others may require as much as 0.6 or 0.8 gm at hourly intervals for 4 or 5 doses Parenteral administration sometimes is required if quinidine is ineffective or not tolerated when given orally.[8] Levine[3] has suggested that atropine sulfate be given hypodermically in addition in those cases in which quinidine slows the ventricular rate but fails to restore normal rhythm using doses of 2 mgm (gr 1/30) one hour after a large oral dose of quinidine The author had a recent experience in a patient with ventricular tachycardia in whom the independent auricular rhythm was considerably slower than the ventricular tachycardia Conversion to normal rhythm occurred only when atropine was given hypodermically after the ventricular rate had been reduced to nearly that of the auricles with quinidine Previous treatment with quinidine alone had failed It is possible that the abrupt speeding up of the sinus rhythm caused it to take over the function of pacemaker Quinidine and magnesium sulfate also have been used successfully in some patients Paroxysmal ventricular tachycardia which occurred in a 46 year-old man is illustrated in Fig 8 This disorder began immediately after the patient had an altercation with his wife The initial slowing produced by quinidine is shown in the second set of tracings Quinidine stopped the tachycardia but a period of dissociation with interference occurred before normal rhythm finally appeared Some time was required for the T waves to become normal possibly because of the prolonged period of tachycardia with embarrassment of the coronary circulation[4] or perhaps *due in part to the large doses of quinidine required*

Paroxysmal auricular tachycardia with auriculo ventricular block is a somewhat uncommon type of paroxysmal rapid heart action which in its character and underlying mechanism seems to be a link between auricular tachycardia of the more usual type and auricular flutter The recent reports of Barker and associates[60] and Decherd and associates[1] have called attention to this disorder whereas only isolated instances had been reported previously This disorder differs from the usual form of supraventricular tachycardia in that atrioventricular block is present and may be constant or variable in degree Although increasing vagal tone by pressure on the carotid sinus may produce the block or increase its degree it does not alter the auricular rate appreciably this is in sharp contrast to the more common type of auricular tachycardia which is either unaltered or stopped abruptly by this measure Furthermore the auricular rate in these patients is much less constant than in auricular

tachycardia of the ordinary type. The auricular rate usually is between 165 and 200 although faster and slower rates have been reported. This is much slower than the auricular rate in most cases of untreated auricular flutter. The electrocardiograms in these patients display auricular deflections which usually are upright and resemble the P waves in records made on the same patient during normal rhythm. Periods of electrical quies-

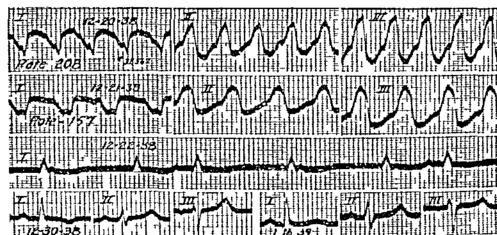


FIG 8 Paroxysmal ventricular tachycardia treated with quinidine. December 20 1938 ventricular tachycardia with rate of 208 per minute. Small auricular deflections seen on the T waves of the second and fourth cycle in lead I. December 21 1938 ventricular tachycardia is still present but the rate has been reduced to 157 per minute with quinidine. December 22 1938 auriculoventricular dissociation with interference; auricular rate 57 per minute, ventricular rate [illegible] per minute. The third and sixth *ventricular beats are responses to auricular impulses which interfere with the idioventricular rhythm.* December 30 1938 normal rhythm with persistent inversion of the T waves in lead I. January 16 1938 normal electrocardiogram except for slight left axis deviation.

This man aged 46 years was admitted two weeks after the onset of the ventricular tachycardia. He was in moderate congestive failure and had grown worse while receiving digitalis. Conversion to normal rhythm resulted from the oral administration of 8.2 grams of quinidine in 47 hours.

cence are seen in the records whereas in auricular flutter the trace never seems to rest on the base line. On the other hand this disturbance of the cardiac mechanism resembles auricular flutter because of the presence of atrioventricular block, the increase in the degree of block which occurs with vagal stimulation, the long duration of the attacks, the slowing of the auricular rate which occurs with quinidine and the occasional conversion of this type of tachycardia to auricular fibrillation.

when digitalis is given. From the clinical point of view paroxysmal tachycardia with A-V block usually causes greater disability than the ordinary form of paroxysmal supraventricular tachycardia because the attacks tend to be of greater duration and the disorder is more resistant to treatment. Most of the observed cases have been patients with diseased hearts and there is evidence to suggest that in some instances this arrhythmia may be precipitated by digitalis. It has occurred in patients with no other cardiac abnormality and in fact in isolated instances has proven fatal[60] an outcome which is most uncommon in auricular tachycardia without block. In those instances which are not the direct result of digitalis that drug is the most beneficial medication so far available. Quinidine quinine and mecholyl have been much less valuable although they are occasionally effective in restoring normal rhythm.

Cardiac Disorders Due to Circus Rhythm

Circus rhythm is a cardiac disturbance in which a wave of activation travels indefinitely in the same direction in a more or less constant closed ring of muscle in such a way that it returns continuously to its point of origin. Mayer, Garrey[63] and Mines each demonstrated circus movements in laboratory preparations and raised the question of their relationship to clinical arrhythmias. Lewis and his collaborators finally established the fact that human auricular flutter and auricular fibrillation were due to circus rhythm. Although other hypotheses have been propounded particularly that of a single ectopic focus discharging impulses in rapid sequence the circus movement theory is quite generally accepted. The recent studies of Rosenblueth and Ramos lend further support to Lewis' hypothesis. It is believed that in auricular flutter and auricular fibrillation there is a single "mother" ring or circuit in the auricular muscle surrounding the great veins and that as the wave of activation travels around this ring of tissue the impulse also spreads centrifugally to activate the other areas of the auricular muscle.

The nature of circus rhythm is shown in Fig. 9. Under normal circumstances if a stimulus is applied to a ring of muscle at a single point the wave of activation spreads evenly and equally in both directions about the circle until the two wave fronts meet at a point opposite and most distant from the starting point. The process of repolarization occurs in the same manner the point activated first being the first area to recover. The wave of activation is therefore followed by a wave of

recovery, the activated muscle being first completely refractory, then partially refractory and finally normally responsive. If a point in the ring of muscle is stimulated at a moment when some portion of the ring is still in the refractory state the wave of activation may spread about one limb of the ring through responsive or partially refractory muscle,

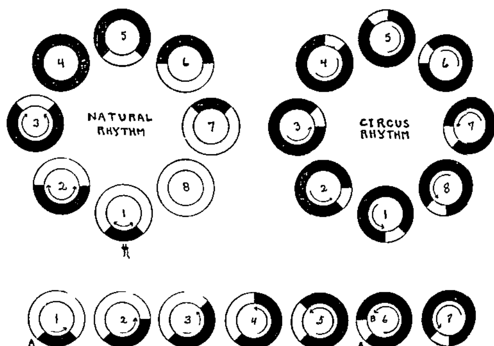


FIG. 9. The mechanism of circus rhythm. The diagram on the left illustrates the course of events when a ring of muscle is stimulated at a single point (1). The black areas indicate muscle which is in contraction and refractory; the white areas correspond to muscle which is in the resting state and not refractory. The contraction wave normally spreads in both directions about the ring and relaxation occurs in the same order. The lower diagram shows the manner of development of circus rhythm. If the contraction wave is blocked at A it will spread in the counterclockwise direction only. If, when the wave reaches B, the refractory period has passed off at A, the wave may then continue to circulate in its own wake, giving rise to the sequence of events diagrammed on the upper right. (From an article by F. N. Wilson.)

whereas its fellow may meet areas of completely refractory tissue and be blocked. Then the unimpeded wave may travel about the circle and since it will not be met by a wave front approaching in the opposite direction it will be able to continue to the point where the block occurred. If the area of block has recovered or if the block is unidirectional the wave of activation is able to pass through this point and

thereby continue about the circuit indefinitely. The circus rhythm thus is established and it will continue so long as the impulse encounters muscle which has recovered or is only partially refractory from the previous wave of activation. The establishment and continuation of circus rhythm are dependent upon three factors, (1) the length of the refractory period, (2) the velocity of transmission of the impulse and (3) the circumference of the ring of tissue. The circus rhythm will develop and persist only if these three factors are so related that the time required for the impulse to make a complete passage about the ring is greater than the duration of the refractory period.

Circus rhythm occurs in all types of clinical heart disease but it is especially associated with rheumatic heart disease with mitral stenosis, thyrotoxicosis and arteriosclerotic heart disease. Paroxysmal auricular fibrillation may be the first evidence of masked hyperthyroidism and careful study with this possibility in mind always should be carried out in any individual with this type of paroxysmal rapid heart action[49]. Circus rhythm commonly occurs in constrictive pericarditis, during severe acute infections such as lobar pneumonia or during poisoning or other toxemias, especially if these disorders occur in elderly persons who already have some coronary arteriosclerosis. Auricular fibrillation or flutter occur uncommonly in patients with syphilitic heart disease, subacute bacterial endocarditis, congenital heart disease or angina pectoris. Transient auricular fibrillation is quite common in association with acute myocardial infarction but it rarely persists after the patient has recovered[67]. Paroxysmal auricular fibrillation also occurs in the absence of any other evidence of heart disease in a group of otherwise healthy young men and in whom fatigue, alcohol or tobacco may be precipitating factors[68, 69].

Auricular Flutter

Auricular flutter is the designation given those examples of circus rhythm in which the ring of muscle about which the impulse is travelling is believed to be relatively large, encircling both the superior and inferior venae cavae. As a result each time the activation wave comes around it encounters muscle which has recovered completely from the passage of the previous impulse. Therefore the circus movement is quite constant in its rate and the pathway it follows. The rate of the circus rhythm usually is between [illegible]o and 380 per minute in auricular flutter which has

not been treated In this disorder the auricular activity produces a continuous regular oscillation of the base line in the electrocardiogram (Fig 30) This oscillation often is described as saw toothed' and is so continuous that it usually is impossible to distinguish the beginning and ending of individual auricular deflections The flutter waves usually are

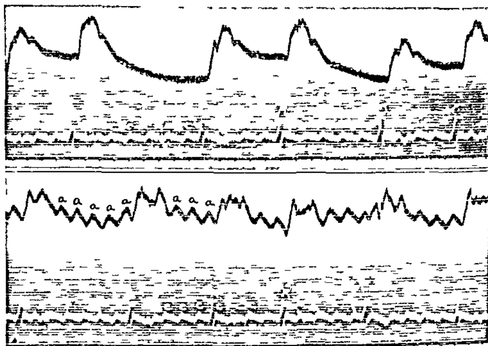


Fig 30 Auricular flutter The electrocardiogram shows auricular flutter with variable relatively high grade A V block (4 1 to 7 1) The constant saw toothed oscillation of the base line which is characteristic of this arrhythmia is easily seen In the upper record the carotid pulse was recorded with the electrocardiogram In the lower record the venous pulse is shown above the electrocardiogram Each circus contraction produces a small wave (a) *in the venous pulse Such rapid regular venous* pulsations often can be detected at the bedside in this disorder (From an article by F N Wilson)

small in lead I and more conspicuous in leads II and III They may be inconspicuous in all of the standard leads and in such cases it may be necessary to take special leads along the right sternal margin or from the esophagus to be certain of the nature of the auricular activity (Fig 31) The auricular oscillations are so constant in their rate and contour that they are practically identical from one examination to the next unless

the patient has received in the interim some medication such as digitalis or quinidine Furthermore most records taken from different patients with auricular flutter show a striking similarity so far as the configuration of the auricular oscillations is concerned probably because the general

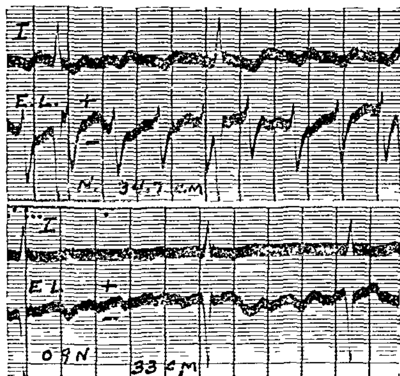


Fig 31 Esophageal leads in auricular fibrillation and auricular flutter In each portion of the illustration the upper record is lead I the lower record is an esophageal lead from the auricular level Above auricular flutter the large auricular oscillations occur at a regular rapid rate and have a constant form from cycle to cycle Below auricular fibrillation the auricular oscillations occur at a more rapid rate and are quite variable in outline from one cycle to the next The observations were made at separate occasions on the same patient

position of the circus pathway about the great veins is much the same in each patient

The ventricles usually are unable to keep pace with the auricles in flutter because the refractory period of the junctional tissues is too long to permit the passage of successive impulses at rates above oo per minute

for any considerable period of time The ventricles respond to a fraction of the auricular impulses producing either 2 1 or 4 1 block or less commonly 3 1, 5 1 or even higher degrees of block The higher degrees of block are seen usually in cases which have been treated with digitalis Auricular flutter with 1 1 responses is seen occasionally in adults[9,11],

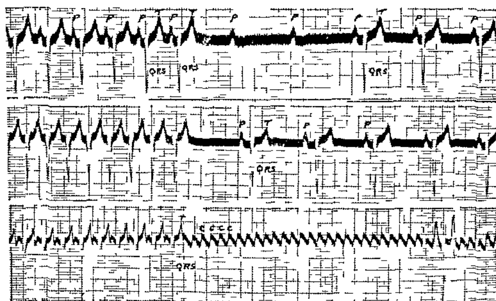


Fig 3 Effect of carotid sinus stimulation in sinus tachycardia paroxysmal supraventricular tachycardia and auricular flutter Upper record sinus tachycardia The auricular rate is reduced and transient heart block is produced in this case A slow normal rhythm follows although there is usually a gradual return to the previous rate Middle record paroxysmal supraventricular tachycardia The tachycardia ends abruptly and slow normal rhythm is restored Note the similarity of the QRS complexes before and after the conversion Lower record auricular flutter A long period of ventricular standstill results but the circus rhythm persists unaltered The electrocardiographic features of the auricular mechanism are particularly well seen during the period of high grade A V block This procedure may be used to confirm suspected cases of auricular flutter (From an article by F N Wilson[7])

and the author has seen one such case in which the 1 1 ventricular response continued uninterruptedly for nearly two hours despite various types of vagal stimulation The degree of block is often variable from moment to moment changing from 2 1 to 4 1 to 3 1 etc this produces a grossly irregular ventricular rhythm which may be differentiated from auricular fibrillation only by means of the electrocardiograph The ventricular deflections are of normal configuration in auricu

lar flutter except in those patients who show aberration of the ventricular response because the rapid ventricular rate permits only incomplete recovery of the ventricular myocardium

The symptoms which appear with the onset of auricular flutter are much the same as those associated with any type of paroxysmal rapid heart action The nature of the underlying heart disease the duration of the arrhythmia and the ventricular rate which develops are major factors in determining these symptoms Profound peripheral vascular collapse and even death have been reported in patients who developed 1 1 responses with extremely rapid ventricular rates Although more difficult to recognize at the bedside than auricular fibrillation there are certain signs which point to auricular flutter There is most commonly 1 block and the ventricular rate is therefore usually between 110 and 190 per minute However if 4 1 block is present the rate will be between 55 and 95 a quite normal range and there will be no rapid heart rate to attract the observer s attention to the underlying disorder The rhythm is perfectly regular if the degree of block is constant and the rate tends to be constant from one observation to the next Alterations in vagal tone which may result from exercise changes in posture carotid sinus stimulation or various drugs may increase or decrease the degree of block Thus in a patient with 1 block and a ventricular rate of 150 vagal stimulation may produce 4 1 block reducing the ventricular rate to 75 exactly one half its initial level The reverse may occur when vagal tone is diminished Such exact doubling or halving of the ventricular rate is always strongly suggestive of auricular flutter The *diagnosis may be suspected first from the observation of rapid full* venous pulsations in the neck associated with a much slower although rapid apical rate or less commonly the rapid auricular flutter may be visualized fluoroscopically as the initial indication of the disorder It is a good rule to suspect auricular flutter in any patient with cardiac failure and a heart rate which is persistently above 135 per minute with a regular rhythm and in the absence of infection or thyrotoxicosis

Auricular flutter must usually be differentiated from paroxysmal tachycardia and sinus tachycardia (Fig 3) The ventricular rate in paroxysmal tachycardia usually is above 180 per minute whereas in auricular flutter and sinus tachycardia it is below that level Vagal stimulation by pressure on the carotid sinus usually terminates paroxysmal tachycardia or does not affect it at all the exception to this is paroxysmal tachycardia with atrioventricular block This measure produces an increase in the degree of block in patients with auricular flutter

with usually an irregular slowing of the ventricular rate and an irregular return to its previous level but with no effect upon the auricular mechanism Sinus tachycardia usually slows gradually and only transiently when vagal tone is increased Exertion, changes in posture and amyl nitrite or atropine usually do not alter the rate of paroxysmal tachycardia but they often induce transient irregularity or abrupt transient changes in the ventricular rate in auricular flutter The ventricular rate in flutter and paroxysmal tachycardia is quite constant from hour to hour whereas sinus tachycardia is apt to display significant fluctuations Large venous pulsations in the neck occurring at the apical rate may be seen in paroxysmal nodal tachycardia, in paroxysmal ventricular tachycardia venous pulsations occurring at a rate slower than and asynchronous with that at the apex may be detected in auricular flutter extremely rapid regular venous pulsations may be visualized sinus tachycardia is not associated with any significant changes in the pulsations of the veins in the neck

Treatment in auricular flutter is directed toward conversion of the abnormal mechanism to normal sinus rhythm This can be accomplished with digitalis in a large percentage of the cases The initial effect of digitalis is to increase the degree of atrioventricular block first to 4 1 responses and then usually to higher or varying degrees of block As more digitalis is given the flutter usually will be converted to auricular fibrillation This occurs when the refractory period of the auricular musculature has been shortened by the digitalis to a point at which the circus movement takes up a newer and shorter pathway This reduction of the auricular refractory period is believed to be motivated through the vagal effect of digitalis If after the onset of auricular fibrillation the digitalis is discontinued normal rhythm usually will appear If normal rhythm does not develop it is still more desirable to have auricular fibrillation than flutter because alterations in vagal tone such as may result from exercise do not cause abrupt changes in the ventricular rate in the former whereas in the latter they may lead to sudden doubling of the ventricular rate with associated palpitation and discomfort An example of paroxysmal auricular flutter occurring in a patient with masked hyperthyroidism is shown in Fig 33 Conversion to normal rhythm was accomplished with digitalis on two occasions Ultimately the patient developed clearly evident hyperthyroidism which was relieved after a subtotal thyroidectomy

Quinidine is used also in the treatment of auricular flutter Its effect is to decrease the rate of conduction in the auricular muscle and to

improve conduction through the atrioventricular node through the partial vagal paralysis which this drug induces The net result of these changes is to drive the auricular rate down to 200 or even to 150 a level at which all of the impulses may be transmitted to the ventricles At times such an effect may make the patient worse For example if he initially had auricular flutter with an auricular rate of 250 per minute and 2:1 block with a ventricular rate of 125 per minute producing an auricular rate of 175 per minute with quinidine with the ventricles assuming the full auricular rate may aggravate the patient s situation However, occasionally, if the quinidine is continued the circus rhythm may be terminated just as in auricular fibrillation with conversion to a normal sinus rhythm This may require large doses of quinidine and is accomplished sometimes more readily if the patient is digitalized first On occasion a patient with auricular fibrillation who is given quinidine, may develop flutter in such a situation it may be necessary to give digitalis to convert the patient back to fibrillation

Auricular Fibrillation

Auricular fibrillation is a circus rhythm which is much less coordinated than auricular flutter Auricular fibrillation is twenty or thirty times as common as auricular flutter and is the most common important arrhythmia which the clinician encounters This disorder is easily produced in experimental animals by mechanical electrical or chemical stimulation of the auricles *The auricular muscle develops a quivering tremulous movement without coordination which has been described as* resembling a ball of wriggling worms It is believed that in this disturbance in contrast with auricular flutter the primary wave of auricular activation is moving about a ring which is relatively small probably encircling only a single one of the caval vessels Not only is the ring smaller but the rate is more rapid usually 400 to 600 per minute and the gap of excitable tissue is narrower As a result of these features the impulse encounters and must find its way through muscle which is only partially recovered from the passage of the previous impulse This makes for a circus movement which varies somewhat in its pathway from cycle to cycle and because of its sinuous meandering course it has a fundamentally irregular rhythm The centrifugal impulses which spread out over the auricle from the central ring are also irregular and follow changing paths with the result that the impulses which reach the junc-

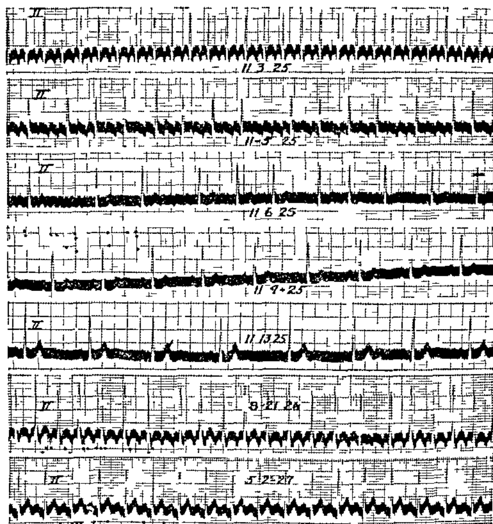


FIG 33 Paroxysmal auricular flutter in masked hyperthyroidism November 3 19 5 auricular flutter with 2 1 A V block The arrhythmia developed 48 hours earlier while the patient was wrestling November 5 19 5 auricular flutter with varying degrees of A V *block patient had received digitalis* November *6 19 5 auricular* fibrillation conversion produced with digitalis November 9 1925 normal sinus rhythm reversion occurred after digitalis was discontinued November 13 19 5 normal sinus rhythm T waves are taller and more upright as result of elimination of digitalis Basal metabolic rate at this time was minus 15 August 21 19 6 recurrence of auricular flutter with 2 1 A V block Conversion to normal rhythm was accomplished by the same procedure employed earlier May 2 19 7 moderate sinus tachycardia distinct clinical manifestations of exophthalmic goitre were present Basal metabolic rate was plus 41 Patient was a student aged 5 years He was completely relieved following a subtotal thyroidectomy

tional tissues also are irregular Just as in auricular flutter the ventricles are unable to develop a rate as rapid as that of the auricles the ventricular rate usually is 90 to 160 per minute although in some instances especially in thyroid crises it may reach 200 or more Records made of the onset

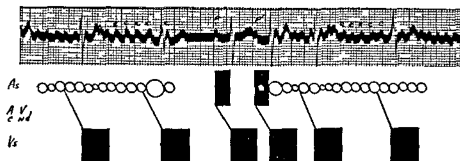


Fig 34 Paroxysmal auricular fibrillation The abrupt offset of an attack is shown after the second ventricular response A single normal beat then occurs It is followed by an auricular premature beat which initiates a new attack of fibrillation Note that the auricular oscillations are inconstant in rate and form This patient had cardiac enlargement and pneumonia (From an article by F N Wilson)

of paroxysmal auricular fibrillation indicate that the disturbance is initiated by an auricular premature beat (Fig 34) This fits in with the hypothesis which Lewis developed regarding the fundamental nature of circus rhythm since an auricular premature beat occurring at a moment when a portion of the auricular myocardium is partially refractory from the preceding normal beat could account for subsequent development of a circus movement in the manner already outlined This also fits with certain clinical observations since patients with mitral stenosis often display frequent premature auricular beats for some time before auricular fibrillation becomes established Individuals with paroxysmal auricular fibrillation commonly have premature auricular beats prior to the onset or immediately after the offset of their paroxysms

The electrocardiogram in auricular fibrillation displays no P waves in the ordinary sense (Figs 34 35 36) There are irregular oscillations of the baseline which represent auricular activity but they are highly variable in outline and grossly irregular in rhythm The oscillations in auricular fibrillation generally are smaller and much less constant from moment to moment than in flutter probably because in the former the impulse is picking its path through a field of partially refractory muscle

and as a result the activation of the primary ring and of the rest of the auricle, which is activated by the centrifugal impulses is so irregular that the sum total of auricular myocardial mass, which is activated at any one time, is quite small The auricular oscillations may be quite large soon after the onset of the arrhythmia, especially in patients with auricular enlargement as in mitral stenosis Such cases are sometimes designated as impure flutter , a term which is not altogether desirable nor is it necessary, since the management of these patients is no different from ordinary auricular fibrillation The oscillations tend to be larger in leads taken along the right sternal margin and particularly from the auricular levels of the esophagus (Fig 31) than in the standard leads In some instances the auricular oscillations may be so inconspicuous in the standard leads as to leave the nature of the auricular activity in doubt, in these cases it may be necessary to employ such special leading to obtain records showing visible deflections of auricular origin As a rule the longer auricular fibrillation has been established the more inconspicuous the auricular oscillations become this is especially true if digitalis has been given for some time The gross irregularity of the ventricular rhythm in this disorder is shown by the highly variable length of successive R R intervals The configuration of the ventricular complexes is normal unless the ventricular rate is so rapid that inadequate recovery produces aberrant responses or unless abnormal QRS complexes are present because of some underlying disorder of the ventricular muscle or specialized conduction tissues such as myocardial infarction or intraventricular block

The *symptoms* produced by auricular fibrillation depend upon its duration the ventricular rate developed and the nature of the underlying heart disease If the ventricular rate is rapid, there may be palpitation weakness and other complaints much as in any type of paroxysmal rapid heart action On the other hand some patients whose ventricular rates are slow, often are completely unaware of the disorder When auricular fibrillation complicates organic heart disease it usually precipitates congestive heart failure which may be alleviated as a rule by controlling the disorder with digitalis or converting it to normal rhythm with quinidine Auricular fibrillation may also signal its onset by the occurrence of peripheral arterial emboli which arise from fragments of intra auricular thrombi broken up by the chaotic auricular action

The clinical diagnosis of auricular fibrillation depends upon observation of the nature of the ventricular activity The ventricles display a

gross irregularity with no fundamental rhythm at all No sequences of any kind occur repeatedly Not only are the cardiac cycles of variable length but the beats are of variable force and the cardiac sounds are of variable intensity depending upon the degree of cardiac filling with each beat This variation in stroke output gives rise to a pulse deficit that is some of the beats fail to put out a sufficient quantity of blood to produce a palpable pulse at the wrist The apex rate then may be 10 to 30 beats faster than the radial pulse rate Although suggestive a pulse deficit is not diagnostic of auricular fibrillation since it may occur with extrasystoles The ventricular rate usually is 90 to 160 but it may be 200 or more and occasionally as slow as 50 or 60 especially in patients who have received digitalis The diagnosis usually is more difficult when the rate is slow because the irregularity is not as pronounced Increasing the ventricular rate by means of exercise amyl nitrite or atropine usually will exaggerate the irregularity The increase in rate under these circumstances is not a reflection of any changes in the auricular activity but rather a sign of decreased vagal tone with improved transmission through the junctional tissues This increase in the irregularity with decrease in vagal tone is a helpful point in differential diagnosis because extrasystolic arrhythmia partial heart block and sinus arrhythmia all become more regular under such circumstances Auricular fibrillation is one of the few disorders in which the cardiac rhythm may be very rapid that is above 150 per minute and irregular The others in this category are paroxysmal auricular tachycardia with atrioventricular block which is rather uncommon and ventricular tachycardia which usually does not show a striking irregularity The occurrence of a pronounced arrhythmia in a young person with a history of rheumatic heart disease should always make one suspect auricular fibrillation and as a corollary it may be said that whenever an electrocardiogram displaying auricular fibrillation and right axis deviation is encountered particularly in patients under 40 years of age mitral stenosis should be suspected The clinical differentiation of frequent premature beats from auricular fibrillation may be difficult especially if the former are arising from multiple foci (Fig 21) Levine has pointed out that with extrasystoles all of the long pauses are preceded by beats of less than normal length but that in auricular fibrillation some of the long pauses will be preceded by cycles which seem to be of average or normal duration and that careful auscultation for this sign may be helpful in distinguishing the two disorders[73]

Digitalis is the drug usually employed to *treat* auricular fibrillation

and as a result the activation of the primary ring and of the rest of the auricle, which is activated by the centrifugal impulses, is so irregular that the sum total of auricular myocardial mass which is activated at any one time is quite small The auricular oscillations may be quite large soon after the onset of the arrhythmia especially in patients with auricular enlargement as in mitral stenosis Such cases are sometimes designated as impure flutter , a term which is not altogether desirable nor is it necessary since the management of these patients is no different from ordinary auricular fibrillation The oscillations tend to be larger in leads taken along the right sternal margin and particularly from the auricular levels of the esophagus (Fig 31) than in the standard leads In some instances the auricular oscillations may be so inconspicuous in the standard leads as to leave the nature of the auricular activity in doubt, in these cases it may be necessary to employ such special leading to obtain records showing visible deflections of auricular origin As a rule the longer auricular fibrillation has been established the more inconspicuous the auricular oscillations become this is especially true if digitalis has been given for some time The gross irregularity of the ventricular rhythm in this disorder is shown by the highly variable length of successive R R intervals The configuration of the ventricular complexes is normal unless the ventricular rate is so rapid that inadequate recovery produces aberrant responses or unless abnormal QRS complexes are present because of some underlying disorder of the ventricular muscle or specialized conduction tissues such as myocardial infarction or intraventricular block

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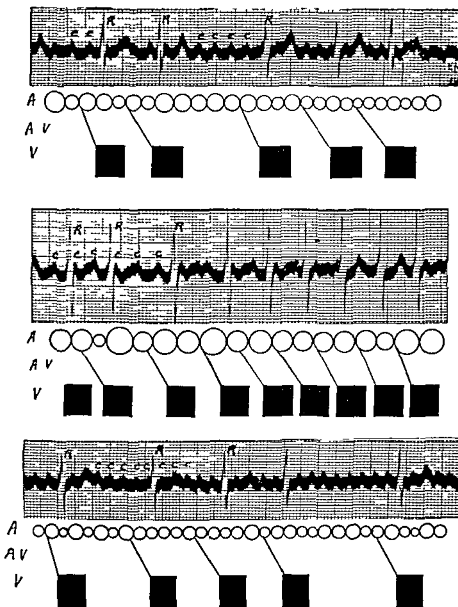


Fig. 35 Auricular fibrillation effect of quinidine and digitalis Upper record is a control the auricular oscillations (c) vary in size and form and their rhythm is distinctly irregular Middle record after quinidine The circus rate has been reduced but the ventricular rate has been increased Lower record after digitalis The circus rate has been increased but the ventricular rate has been decreased The diagrams of the cardiac mechanism show at A the relative size and rate of the circus movement All records were taken on the same patient using electrodes upon the upper and lower sternum to record large auricular oscillations (From an article by F N Wilson)

This is especially true in those cases in which the therapeutic aim is only to control the ventricular rate but not to induce a return to normal rhythm The reduction of the ventricular rate usually is the result of vagal stimulation by the drug and the direct effect of digitalis upon the junctional tissues with consequent further depression of atrioventricular conduction (Fig 35) Digitalis is not employed because of its effect upon the circus rhythm because its direct effect upon auricular muscle and its indirect effect upon the circus movement through its stimulation of the vagus largely counterbalance each other If it alters the circus rhythm at all it tends to increase the circus rate through its vagal effect Although normal rhythm may appear in a patient who has received digitalis such a turn of events is probably accidental because the general effect of the drug is to perpetuate the circus movement As the ventricular rate is reduced the heart becomes more efficient the pulse deficit usually disappears almost entirely and the patient is considerably improved The expected slowing occasionally fails to appear this is especially apt to be the case in hyperthyroidism when severe infection is present or when intractable terminal congestive heart failure has developed

From time to time a patient who has been known to have auricular fibrillation and who has been given digitalis will display an unexpectedly regular rhythm (Fig 36) The ventricular rate usually is 50 to 60 per minute These patients will be found to have an independent ventricular rhythm which is different from the more classical type of complete atrioventricular heart block in that the ventricular rate is more rapid and usually not so absolutely regular This disorder is a sign of serious digitalis intoxication and the rate is more rapid than in the classical form of complete heart block because of the tendency of digitalis to enhance the inherent rate of the lower nodal and higher ventricular centers If more digitalis is given the ventricular rate becomes more and more rapid until ultimately ventricular tachycardia or fibrillation occur Unless the clinician is aware of this effect of digitalis in auricular fibrillation he may assume that his treatment has produced normal sinus rhythm He may be inclined to continue the digitalis for other reasons and the net result will be a gradually increasing ventricular rate He may give still more digitalis to control this incipient tachycardia and the final result may be fatal intoxication It is essential that this type of complete heart block due to digitalis in patients with auricular fibrillation be recognized and electrocardiographic confirmation of suspected cases is always desirable

the circus movement is concerned, because the former tends to perpetuate and the latter to terminate the arrhythmia This drug also tends to paralyze the vagus thereby improving conduction in the junctional tissues Therefore when quinidine is given the auricular rate is decreased, and the ventricular rate is increased (Fig 35) an effect which has led to the statement that when the drug is given the patient is made worse temporarily However when a sufficient dose has been given

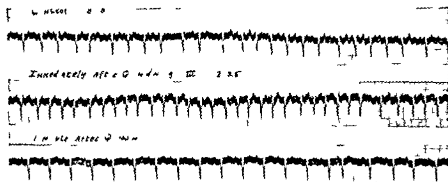


Fig 3 Auricular fibrillation with conversion to normal rhythm after quinidine Upper record auricular fibrillation with ventricular rate 1 4 per minute Middle record immediately after quinidine 0 2 gm (3 gr in) was administered intravenously ventricular rate has risen to 163 per minute Lower record [illegible] minutes after administration of quinidine normal sinus rhythm except for occasional auricular extrasystoles

conversion to normal rhythm usually occurs (Fig 37) The dose required varies greatly from one patient to the next The most satisfactory plan usually is to give doses of increasing size (0 gm 0 , gm 0 4 gm etc) at intervals of two or three hours observing the patient before each successive dose In this way the drug can be discontinued whenever conversion to normal rhythm has occurred Recent observations have shown that this dosage plan results in a cumulative effect which is not obtained by divided doses of equal size The drug may cause some disagreeable symptoms particularly nausea vomiting diarrhea or tinnitus There is some hazard of causing emboli to be broken off thrombi which may be present in the auricular appendages especially in patients who have been fibrillating for a long time or who have marked auricular dilatation Quinidine can alter intraventricular conduction and when extensive myocardial disease is present this drug must be used with par

Quinidine is useful in selected cases in converting auricular fibrillation to normal sinus rhythm It is indicated particularly in those patient whose underlying disorder is reversible or only transient as in hyperthyroidism acute febrile illnesses and in acute cardiac injuries which

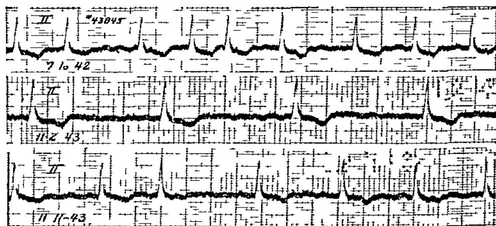


Fig 36 Auricular fibrillation with complete heart block resulting from excess digitalis July 16 194 auricular fibrillation ventricular rate 133 per minute November 2 1943 auricular fibrillation is still present Note the absence of P waves and the inconstant variable oscillation of the baseline The ventricular rate is 58 per minute the ventricular rhythm is completely regular indicating that the ventricles are no longer responding to the fibrillating auricles but have established an independent rhythm This disorder usually is a sign of serious digitalis intoxication November 11 1943 after digitalis was omitted for nine days Auricular fibrillation with a ventricular rate of 95 per minute is present A completely irregular ventricular rhythm has reappeared The QRS complexes have the same form in all three records indicating that the idioventricular rhythm arose above the bifurcation of the His bundle This woman aged 39 years had rheumatic heart disease with mitral stenosis and a toxic adenomatous goitre

have initiated auricular fibrillation It is especially indicated when paroxysmal auricular fibrillation occurs in the absence of any other evidence of heart disease On the other hand if the cardiac abnormality which predisposes to the fibrillation is a permanent one as in mitral stenosis even though the rhythm may be restored to normal the circus rhythm usually will recur because the disorder which initiated the auricular fibrillation still is present The indications for quinidine must be weighed carefully and individually with each case Quinidine decreases the rate of conduction in the auricular musculature and also increases the length of its refractory period These two effects oppose each other, so far as

the lesion that is the side activated late displays initial positivity because of the unopposed boundary which moves toward the involved side from the intact side early in the QRS interval

If two points are selected on the free wall of one of the ventricles one on the epicardial surface (point A) and the other directly beneath it on the endocardial surface (point B) the potential variations occurring at other points in the heart will affect A and B equally since all such other points are practically equidistant from A and B Therefore any potential differences measured between A and B will be due to what happens in the muscle which separates them When the subendocardial muscle is activated B becomes negative and A becomes positive This relation between the two points persists as the wave of activation moves through the intervening muscle toward A but as soon as it reaches that point A and B are at the same potential Therefore if an exploring electrode is placed over such an epicardial point A and is paired with some distant reference point which has a negligible potential the time of arrival of the impulse at point A will be indicated by a sudden shift of the trace from positive to negative this is the intrinsic deflection When the activation wave reaches the epicardial electrode the boundary between acting and resting muscle disappears and the electrode then displays the potential of the underlying ventricular cavity which is negative this accounts for the sudden drop in potential which characterizes the intrinsic deflection The amplitude of the intrinsic deflection is a rough measure of the potential difference between endocardial and epicardial surfaces at the point being explored Recent considerations suggest that the point at which the intrinsic deflection terminates probably coincides more accurately with the instant of activation of subepicardial muscle beneath the exploring electrode than the point at which the intrinsic deflection begins[7]

Leads such as that mentioned above in which the exploring electrode placed on the epicardium is paired with a reference or indifferent electrode placed at some distant point are designated as unipolar because the potential variations at the ventricular surface are so much larger than those at the distant point that the latter may be disregarded Such leads from the ventricular surface are designated as unipolar direct leads They display QRS complexes which consist of two parts divided by the intrinsic deflection That portion of the QRS complex which precedes the intrinsic deflection is produced by muscle which is activated before that portion of the myocardium which is in contact with the exploring electrode whereas the deflections following the intrinsic deflection are

trode an abrupt shift to negative potential occurs and persists as the wave front moves away lasting until it reaches the opposite end of the fibre where it dies away The sudden shift of the trace from positive to negative (R-S movement) is called the intrinsic deflection, it indicates the time of arrival of the impulse beneath the exploring electrode[9]

Excitation of the Ventricular Muscle

For purposes of illustrating the order of excitation of the ventricular muscle the ventricles may be visualized as a hollow sphere, open at one end (corresponding to the atrioventricular groove, the auricles and the large vessels) and divided into two cavities by a muscular septum Normally the impulse comes down through the junctional tissues to the main stem of the His bundle and spreads through the bundle branches and into the ramifications of the Purkinje network This system is elaborated so that many points of subendocardial muscle are activated simultaneously and therefore in the initial stage of ventricular activation both ventricular cavities are lined with active muscle The septum had always been considered activated simultaneously half from one side and half from the other so that the two waves of activation opposed and cancelled each other Recent studies of the potential variation of the right ventricular cavity indicate that chamber is initially positive for a brief period of time probably because the left half of the septum is activated slightly earlier than the right thereby producing a boundary which is moving toward the right ventricular cavity very early in the QRS interval[6, 81, 8] However the right half of the septum is activated soon thereafter and the opposing wave fronts are present in the septum from that point on Except for this initial brief interval when an unopposed wave front is moving from the left side of the septum the spread of the impulse through the ventricular muscle is from within outward away from the ventricular cavities Because the ventricular cavities are on the negative side of all boundaries they display a negative potential throughout the QRS interval with the exception of the right cavity as noted above A record of the potential variation of the right ventricular cavity will show a tiny initial positive deflection and then a large deep negative deflection, a similar record from the left ventricular cavity will show only a large deep negative deflection (QS wave) If the continuity of one of the bundle branches is interrupted so that one side of the septum is activated earlier than the other, the ventricular cavity on the side of

parable to that obtained in observations on animals using direct leads Precordial leads often detect lesions which are beyond the range of the standard leads Precordial leads are based upon principles quite unlike the standard leads and should never be looked upon as just a fourth lead in addition to the standard three The standard leads are bipolar leads employing two electrodes which are roughly equidistant from the heart *The potential variations at one or the other of these electrodes* may dominate the final record if one happens to be larger than the other but inspection of the tracing will not indicate this fact Records employing the standard leads do not display an intrinsic deflection Because the electrodes are at some distance from the heart they are apt to display the average potential variation over a large area of the surface of the heart On the other hand the potential variations of a precordial electrode are determined largely by those of the zone of ventricular muscle nearest the electrode Furthermore in man the potential variations of the precordium are three to five times as large as those of the extremities The reason for this is that the trunk acts as a volume conductor currents which are generated by the heart are short circuited by the body tissue and although some current flows in every part of the trunk it diminishes rapidly *as one moves away from the heart toward the shoulders and the* pelvis[3] On the other hand the arms and legs act as linear conductors and there is no significant difference in the current at the upper arm at the forearm or at the wrist

In order to take precordial leads the exploring electrode which is placed on the chest must be paired with an indifferent or reference electrode placed at a point relatively distant from the heart One of the extremities is commonly employed as the reference point and the leads are then called CR CL or CF leads depending upon whether the right arm the left arm or the left leg is used If the precordial leads are to be considered semi direct leads from the surface of the heart the potential variations of the reference electrode must play a negligible role in determining the outline of the final record This is not always the case when *one of the extremities is used*[91, 8] *In order to eliminate* so far as possible the confusion which may result from pairing the precordial electrode with one placed on one of the extremities Wilson and his associates[46, 87] devised an artificial ground or central terminal which is merely the meeting point of three lead wires connected through equal resistances of 5 000 ohms each to the three extremities used in taking the standard leads Wilson has elaborated recently upon some of the theoretical considerations which led him to choose the central terminal as a reference

due to muscle activated later than that upon which the electrode is resting Consequently the outline of the QRS complexes in such leads is influenced greatly by the time of activation of the muscle beneath the exploring electrode and in turn by the relative thickness of that portion of the heart Where the muscle is thin the time required for the impulse to traverse the myocardium is relatively short, and there will be large areas of the heart elsewhere which will be activated later than the point in question Over such a thin area the QRS complex will consist of a small narrow R wave and a deep broad S deflection with the intrinsic deflection occurring early in the QRS interval Where the muscle is thick the time required for complete activation is greater and only small areas of muscle elsewhere will be activated later than the point being considered Over such a thick zone the R wave will be broad and tall and the S wave will be small with the intrinsic deflection late in the QRS interval If the exploring electrode is placed over that zone of the myocardium which is the last to be activated the intrinsic deflection terminates the QRS interval and no S wave occurs

Records from some epicardial areas display small Q waves preceding tall broad R deflections followed in turn by small or absent S waves It is believed that all parts of the subendocardial muscle are not activated simultaneously If an exploring electrode is placed over some zone of the ventricular wall where the subendocardial muscle is activated relatively late it may display the initial negativity of the ventricular cavity resulting from the earlier activation of other zones of subepicardial muscle and transmitted through the resting muscle upon which the electrode is situated Such records are particularly apt to be derived from the thicker portions of the free wall of the left ventricle Another explanation for such small initial Q waves is that they may be due to the initial negativity of the left ventricular cavity which results from early activation of the left half of the septum

Unipolar Precordial Leads

Direct leads cannot be taken clinically, and most of our knowledge regarding them comes from the study of experimental animals This information had been supplemented recently by that gained from intracardiac leading[80, 81, 8] Precordial leads are more nearly related to direct leads than any others which are practicable clinically It is because of this that they are often of so much more value than the standard leads Furthermore leads from the precordium furnish data more nearly com

intrinsic deflection occurs late in the QRS interval these characteristics means that the ventricular muscle beneath the electrode is relatively thick and the activation wave reaches the epicardium relatively late The intrinsic deflection is usually 0 02 to 0 03 second later in the QRS interval in leads V_5 and V_6 than it is in leads V_1 and V Lead V_4 usually is of transitional form and is probably an admixture of the potential variations over the right and left ventricular surfaces nearest the electrode However the exact location and range of this transitional zone are quite vari

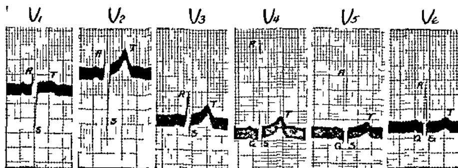


Fig 38 Normal precordial electrocardiogram The R deflection grows taller and the S wave grows smaller as the electrode is moved from lead V to lead V The R wave again decreases in size in leads V and V The T wave is upright in all leads except lead V in which it is diphasic The Q and S deflections over the left precordium are relatively small In this case lead V represents the transitional zone (From an article by F N Wilson in Stroud's Diagnosis and Treatment of Cardiovascular Disease F H Davis Company Philadelphia)

able from patient to patient this fact is one of the most significant reasons for taking multiple precordial leads rather than a single record from a point somewhere near the apex The factors which influence the position and width of the transitional zone are still unclear but the relative position of the heart in the thorax and cardiac enlargement are important in this regard Any system for recording multiple precordial leads must cross the transitional zone because much of the value of such leading depends upon the contrast in form of the electrocardiograms recorded from the right and from the left of this zone If the standard six precordial leads fail to cross the transitional zone additional leads should be taken to the right or left of the usual points whichever seems indicated The T waves usually are upright in all of the precordial leads in the normal person although the T waves may be inverted in lead V_1 and rarely in lead V

point[88] Such a central terminal displays at every instant the mean potential of the three extremities and its potential variations have been found to rarely exceed 0.3 millivolt. When such a reference point is used it *may be considered to have a practically zero potential throughout the* cardiac cycle and precordial leads taken in such a manner may be considered practically unipolar semi-direct leads. Furthermore, with such an indifferent electrode nearly unipolar leads may be taken from any point on the body, whether it be on the trunk or the extremities or in the esophagus.

When an exploring electrode is moved across the precordium through a sequence of points the series of records obtained depicts the potential variations of the various parts of the anterior ventricular surface. It is now the generally accepted practice to take multiple precordial *lead* from six precordial points specified by the Committee of the American Heart Association for the Standardization of Precordial Leads[89]. The *first* of the six points is at the right sternal margin in the fourth intercostal space and the *second* is at the left sternal margin at the same level. The *fourth* point is at the intersection of the left mid-clavicular line and a horizontal line at the level of the cardiac apex. If the apex cannot be located, the horizontal level of the fifth intercostal space at the left mid-clavicular line is used. The *third* point is midway between the second and fourth points. The *fifth* is in the anterior axillary line and the *sixth* is in the mid-axillary line, both on a horizontal line which is a continuation of the apical level around the left lateral thorax. Precordial leads from these points using the central terminal as the indifferent electrode are designated as V_1, V_2, V_3, V_4, V_5 and V_6. Additional records taken from other points over the thorax may be designated to indicate their origin on the chest or their relation to these more usual ones, i.e. V_E from the tip of the ensiform cartilage, V_7 from the left posterior axillary line at the same horizontal level as V_5 and V_6, V_8 from the left infra*scapular region, V_{4R} corresponding to V_4 but in the right mid clavicular* line.

An example of the precordial electrocardiogram in a normal individual is shown in Fig. 38. It will be seen that the records from the right precordium (leads V_1 and V_2) show small sharp R waves, large broad S deflections and an intrinsic deflection which occurs early in the QRS interval; these features indicate that the ventricular muscle underlying the electrode at these points is thin and its epicardial surface is activated relatively early. Records from the left precordium show taller broader R waves, small or absent S deflections, small or absent Q waves and the

leads and are therefore, of considerable help in understanding many electrocardiographic problems In general the extremity displays the potential variations of that part of the heart which faces it The right arm develops the potential variations of that part of the heart which faces the right shoulder Lead V_R usually shows slight initial or final positivity or both but it is usually negative throughout the greater part of the QRS interval Its outline may be designated as Qr rS or rSr This is because the negativity of the ventricular activities is transmitted through the large orifices at the base of the heart toward the right shoulder with relatively little cardiac muscle interposed The left arm displays the potential variations of that part of the heart which faces the left shoulder and the left leg displays the potential variations of the diaphragmatic aspect of the heart but both leads V_L and V_F appear to be influenced greatly by the position of the heart As the heart becomes more horizontal or rotates about its long axis so that the left ventricle faces the left shoulder and the right ventricle comes to lie below the left lead V_L resembles the potential variations recorded from the epicardial surface of the left ventricle in direct leads in dogs and in precordial leads V and V_6 in humans i e it has an Rs qR qRs or R outline on the other hand lead V_F displays potential variations such as are recorded from the epicardial surface of the right ventricle in direct leads in dogs and in precordial leads V_1 and V in humans i e it has an rS form On the other hand as the heart becomes more vertical or rotates about its long axis to bring the left ventricle behind or below the right the character of the potential variations of these two extremities is reversed and lead V_L resembles leads V_1 and V while V_F resembles leads V and V_6[9]

The relations between the unipolar limb leads and the precordial leads have been used to define six electrocardiographic positions of the heart[9]

1 Vertical position
   a The ventricular complexes of lead V_L resemble those of V_1 and V
   b The ventricular complexes of lead V_F resemble those of V and V_6
2 Semivertical position
   a The ventricular complexes of lead V_F resemble those of leads V and V_6
   b The QRS deflections of V_L are small and the positive and negative deflections are of equal size

In normal infants and children the T waves may be inverted in all leads as far to the left as V_4 or V_5 but with advancing years they become progressively upright, the progression moving from left to right[90] The range of the size of the deflections of the ventricular complex in multiple precordial leads for a group of normal individuals studied by Kossman and Johnston[91] is shown in Table I (see in section Elements in the Electrocardiogram) The major characteristics to bear in mind are that in the normal precordial electrocardiogram the R wave become progressively larger and the S wave smaller with the intrinsic deflection later in the QRS interval as the exploring electrode is moved from the right to the left precordium although the R wave usually is smaller in leads V_5 and V_6 than in V_4[9]

Unipolar Limb Leads

The potential variations of the individual extremities can be recorded by using as an indifferent electrode the same central terminal used in taking the unipolar precordial leads and placing the exploring electrode on each of the extremities in turn instead of on the precordium These records are designated lead V_R (right arm) lead V_L (left arm) and lead V_F (left leg) For greater convenience and in order that these unipolar extremity leads may be taken with the galvanometer at the normal sensitivity Goldberger introduced a modification whereby the central terminal is disconnected from that extremity upon which the exploring electrode is placed[93] Unipolar limb leads taken in this manner are called augmented and usually are labelled aV_R aV_L and aV_F their configuration is exactly the same as that of records taken with Wilson's original technique The unipolar limb leads are the parts of which the standard leads are composed Wilson and his associates have discussed the relation of the standard leads and the unipolar limb leads at length[6, 83, 87, 9, 94] It may be pointed out here merely that lead I consists of the potential variations of the left arm (V_L) minus those of the right arm (V_R) lead II consists of the potential variations of the left leg (V_F) minus those of the right arm (V_R), lead III consists of the potential variations of the left leg (V_F) minus those of the left arm (V_L)

It is unlikely that the unipolar limb leads will displace the standard limb leads since so much of our knowledge of electrocardiography is based upon the latter However experience with these leads has shown that they are a link between the precordial leads and the standard limb

when there is preponderant hypertrophy of one of the ventricles In more complex situations as when multiple myocardial infarcts are present, no good correlation between the unipolar limb leads and the precordial leads is possible because the extremities are apt to show mixtures of potential variations of many types which are occurring in many local areas

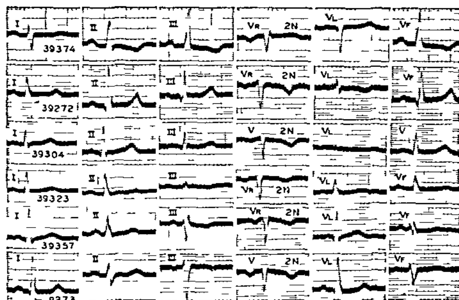


Fig 39 The standard leads and unipolar limb leads of six patients arranged according to the position of the mean electrical axis of QRS The unipolar limb leads were taken with the galvanometer at twice the normal sensitivity (N) Mean electrical axis of the upper record is approximately plus 90 that of the lowest record is minus 30 Those intervening are arranged in increasing order of counterclockwise rotation of the mean electrical axis Assuming that the QRS deflections of the precordial leads had they been taken would have been of the normal type the heart was in the vertical position in the first case in the semivertical position in the second and third in the intermediate position in the fourth in the semihorizontal position in the fifth and in the horizontal position in the sixth case (From an article by Wilson and associates[9])

The unipolar limb leads are of particular value in the diagnosis of myocardial infarction ventricular hypertrophy and bundle branch block The potential variations of myocardial infarcts which are anterolateral in location are transmitted to the left arm (V_L) whereas those of infarcts which are posterior or diaphragmatic in location are transmitted

3 Intermediate position
   a The ventricular complexes of leads V_L and V_F are similar in form and size and like those of leads V_5 and V_6
4 Semihorizontal or semitransverse position
   a The ventricular complexes of lead V_L resemble those of leads V_5 and V_6
   b The QRS deflections of lead V_F are small and the R and S waves are of equal size
5 Horizontal or transverse position
   a The ventricular complexes of lead V_L resemble those of leads V_5 and V_6
   b The ventricular complexes of lead V_F resemble those of leads V_1 and V_2
6 Indeterminate position
   a There is no obvious relationship between the ventricular complexes of the limb leads and those of the precordial leads

The standard and unipolar limb leads of six patients are reproduced in Fig 39 to illustrate these various electrocardiographic positions Those *at the top of the figure display the most vertically placed heart* and those at the bottom show the most horizonally placed heart When the electrocardiogram is normal there is a close correlation between the mean electrical axis (the average direction of spread of the wave of activation over the ventricles) and the electrocardiographic position but as will be seen in later discussions this relation does not always hold when the heart is abnormal

The correlation between the anatomical and electrocardiographic positions of the heart is imperfect and a change in one is not necessarily accompanied by a change in the other For example in bundle branch block the distribution of potential variations of various types over the heart may change with the onset of the block thereby altering the electrocardiographic position without affecting the anatomical position It is important to bear in mind that those parts of the heart which determine the form of the unipolar limb leads and those which determine the form of the precordial leads are not the same A fairly good correlation between these two types of leads can be demonstrated when potential variations of a single type occur simultaneously over large areas of the right ventricle, and potential variations of a different character occur simultaneously over large areas of the left ventricle This is apt to be the case when the heart is normal when bundle branch block is present, or

the impulse travels from the main stem of the His bundle down the uninjured branch and it must then pass through the muscle of the interventricular septum to reach the Purkinje system on the injured side In this situation then all of the septum is activated in one direction rather than one half from the right and one half from the left as it is normally When bundle branch block is present the first portion of the QRS complex represents the normal ventricle which is activated at the normal time in the QRS interval The second part of the QRS complex represents chiefly, the abnormal ventricle whose activation is delayed by a few hundredths of a second If right bundle branch block is present the initial part of the QRS complex represents the left ventricle and may be designated the levocardiogram[17] When left bundle branch block is present the early portion of the QRS complex represents the right ventricle and may be called the dextrocardiogram[1] The normal electrocardiogram is the algebraic sum of the levocardiogram and the dextrocardiogram and it is therefore a bicardiogram[13] In general in bundle branch block the order of recovery from the active state (repolarization) is substantially the same as the order of activation (depolarization) Consequently the two ventricles recover asynchronously and that ventricle which is activated first recovers first whereas that chamber which is activated last recovers last[96] As a result of this whenever the QRS complex *is considerably altered in form by bundle branch block the T* wave also is modified

Right Bundle Branch Block

The factors which determine the form of the electrocardiogram in right bundle branch block stand clear if the sequence of activation of the ventricular muscle in this condition is understood (*Fig 40*) The initial spread of the impulse from the intact left bundle branch is through the interventricular septum in a left to right direction All of the septum is activated from the left side During this initial phase the cavity of the left ventricle displays a negative potential since the boundary is moving away from it and the right ventricular cavity has a positive potential because the boundary in the septum is moving toward it In the second phase the apex and lateral free wall of the left ventricle are activated the impulse arriving in this area at the normal time The movement of the activation wave through these structures makes the potential of both the left and right ventricular cavities negative since in each instance the

to the left leg (V_F). Occasionally infarcts in unusual locations such as high anterolateral lesions may produce more striking changes in the unipolar limb leads than in either the standard limb leads or the standard precordial leads. The unipolar extremity leads help to clarify situations in which the clinical picture and the precordial leads suggest preponderant hypertrophy of one ventricle and yet the standard leads fail to show the expected type of axis deviation. An unusual position of the heart disclosed by the unipolar limb leads usually will be found to account for this disparity.

Intraventricular Block

It is probable that no other problem in electrocardiography has been more fraught with confusion than that of intraventricular block. There is still disagreement about many aspects of this problem, and there are some observers who question the existence of the His bundle and its branches in humans[4]. The present discussion will be based upon the modern conception of the electrocardiographic diagnosis of bundle branch block which is grounded upon numerous fundamental experimental and clinical observations[6, 81, 8, 83, 92, 96, 9, 98, 99, 100]. Whether or not the branches of the His bundle are demonstrable histologically, there is strong evidence that they exist physiologically and play an important role in atrioventricular conduction. For example many records of transient bundle branch block have been reported with the defect present one day and gone the next. Furthermore electrocardiograms, showing alternating complete and incomplete bundle branch block (Figs 44 and 45) and complete bundle branch block alternating with normal conduction (Fig 42) have been recorded. Such phenomena can be explained only by assuming the presence of a single small area or strand of tissue which plays a decisive part in the spread of the impulse in the heart and they cannot be attributed logically to some instantaneous change in the condition of so large a muscle mass as the ventricular myocardium as a whole. Bundle branch block is of interest and significance in the study of the form of the electrocardiogram because it permits the isolation of the contribution made by either ventricle during the early part of the *QRS interval. Furthermore the study of human and experimental* bundle branch block permits us to test the hypotheses which have been developed concerning the spread of activation over the heart.

When the continuity of one of the bundle branches is interrupted

The standard leads show certain characteristic features in right bundle branch block (a) the QRS interval measures 0 1 sec or more in duration (b) the QRS complex in lead I is biphasic or triphasic that is it consists of an R and S deflection which may or may not be preceded by a small Q wave, (c) the final deflection of the QRS complex in lead I

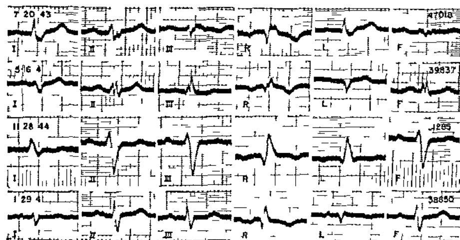


Fig 41 Various types of right bundle branch block Upper record (No 4,018) common type of right bundle branch block broad slurred S waves are present in leads I and II This patient had arteriosclerotic heart disease Second record (No 39837) less common form of right bundle branch block small P waves and broad S deflections are present in lead I broad notched R waves are seen in lead III This patient had congenital heart disease possibly Lutembacher's syndrome Third record (No 51285) least common form of right bundle branch block the S deflection in lead I is relatively small whereas the S waves in leads II and III are unusually prominent This patient had arteriosclerotic heart disease Fourth record (No 388 0) incomplete right bundle branch block Patient had calcific mitral stenosis and aortic insufficiency The precordial electrocardiograms of the first three patients were practically identical in outline

is a broad slurred or notched rather shallow S wave The unipolar limb leads usually display a prominent broad notched or slurred R or R deflection occurring late in the QRS interval in lead V_1 The configuration of leads V_L and V_F depends largely on the electrocardiographic position of the heart but one or the other usually consists of a prominent R deflection and a broad S wave resembling the leads from the left precordium except that the R wave usually is larger in the latter Right bundle branch block has been classified into three types according to

boundary is moving away from the points in question Finally the lateral, free wall of the right ventricle is activated at a time considerably later than normal Passage of the wave of activation from the endocardial to epicardial surfaces in this zone maintains the negativity of both ventricular cavities An electrode placed over the lateral wall of the right ventricle records an initial small R wave the initial positivity of the right ventricular cavity being transmitted to it Then there follows a small

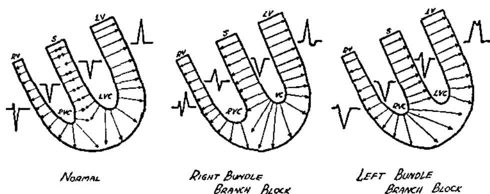


Fig 40 The spread of ventricular excitation when intraventricular conduction is normal (A) and in right (B) and left (C) bundle branch block When conduction is normal half of the septum is activated from the left and half from the right both ventricular cavities are negative throughout the QRS interval In right bundle branch block all of the septum is activated from the left and the right ventricular cavity is initially positive In left branch block all of the septum is activated from the right, the left ventricular cavity is initially positive

negative deflection resulting from the activation of the lateral wall of the left ventricle Lastly there is inscribed a large final upward deflection (R′) which represents the spread of the impulse through the free wall of the right ventricle and the right half of the septum A QRS complex of this form is always recorded in lead V_1 in human right bundle branch block An electrode placed over the lateral wall of the left ventricle records an initial large upward deflection due to activation of the relatively thick left ventricular wall toward the electrode and finally a broad slurred rather shallow S wave which results from the late activation of the free wall of the right ventricle The activation of the septum *from the left side often produces a tiny initial Q wave in records* taken from the lateral wall of the left ventricle Records of this general contour are obtained routinely in leads V and V_6 in human right bundle branch block

The standard leads show certain characteristic features in right bundle branch block (a) the QRS interval measures 0 1 sec or more in duration, (b) the QRS complex in lead I is biphasic or triphasic that is it consists of an R and S deflection which may or may not be preceded by a small Q wave (c) the final deflection of the QRS complex in lead I



Fig 41 Various types of right bundle branch block Upper record (No 47018) common type of right bundle branch block broad slurred S waves are present in leads I and II This patient had arteriosclerotic heart disease Second record (No 39837) less common form of right bundle branch block small R waves and broad S deflections are present in lead I broad notched R waves are seen in lead III This patient had congenital heart disease possibly Lutembacher's syndrome Third record (No 51285) least common form of right bundle branch block the S deflection in lead I is relatively small whereas the S waves in leads II and III are unusually prominent This patient had arteriosclerotic heart disease Fourth record (No 38350) incomplete right bundle branch block Patient had calcific mitral stenosis and aortic insufficiency The precordial electrocardiograms of the first three patients were practically identical in outline

is a broad slurred or notched rather shallow S wave The unipolar limb leads usually display a prominent broad notched or slurred R or R' deflection occurring late in the QRS interval in lead V_R The configuration of leads V_L and V_F depends largely on the electrocardiographic position of the heart but one or the other usually consists of a prominent R deflection and a broad S wave resembling the leads from the left precordium except that the R wave usually is larger in the latter Right bundle branch block has been classified into three types according to

the outline of the stndird leids These hive been designited is (1) common (2) less common ind (3) least common, and examples of each are shown in Fig 41 The conduction disturbance is identical in each case shown in the upper three records, the precordial electrocirdiogrim in each case was chiricteristic of right bundle branch blocl and all were similar These records differ from each other because of variations in the position of the heart In each case a prominent, slurred S deflection is present in leid I and a broad notched or slurred lite R deflection is seen in leid V_1 The upper record in Fig 41 is the most common type of right bundle brinch blocl Leid V_L resembles leids V_5 and V_6 in this condition ind leid V_F is small, the heirt is, therefore in the semi hori zontil position The second record illustrates the less common form of right bundle branch blocl ilthough it was considered the classical form of this disorder for miny yeirs In this cise it is lead V_F which shows the prominent R ind smill S deflections instead of lead V_L as in the previous eximple Leid V_1 is smill ind chiefly negitive in direction Here the heart was in a semi-vertical position, but the unipolar limb leads show some atypicil feitures which probibly resulted from the congenitil heirt disease which was ilso present A somewhat more clissical example of right bundle branch block in a semi verticilly plhced heart is shown in Fig 42 The leist common type of right bundle brinch block is illustrated in the third record in Fig 41 The S wive in lead I is so inconspicuous and the S deflections in leads II ind III are so broid ind deep that it first glance this record suggests left bundle branch block The precordial leids excluded that possibility Q or S deflections in leid I are rarely encountered in left bundle branch blocl even when they ire as small as in the cise here unless myocardial infarction involving the septum is present ilso[101] Leids V_L and V_F in this third case ire not chiricteristic of the potential virintions of either the right or left ven tricle but the relatively late R wave in lead V_L and the eirly intrinsic deflection in lead V_F suggest thit the potential varintions of the left arm are dominited by areas of the heirt which ire ictivated late and those of the left leg by zones ictivated early in the QRS intervil The heirt apparently was in i vertical position A somewhit similir exiample is illustrited in Fig 43

The precordial leids in right bundle brinch blocl show several chiracteristic features The QRS intervil is 0 12 sec or longer and often this interval ippeirs longer in leids V_1 ind V than in the stndird leads Leid V_1 ind often leids V ind V_1 (ensiform process) shows

the most significant and diagnostic changes In this lead the QRS complex consists of a small initial R wave followed by an S deflection which may be embryonic* small or large succeeded by a large late R wave The tiny initial R reflection is due to the activation of the septum from left to right and reflects the initial positivity of the right ventricular

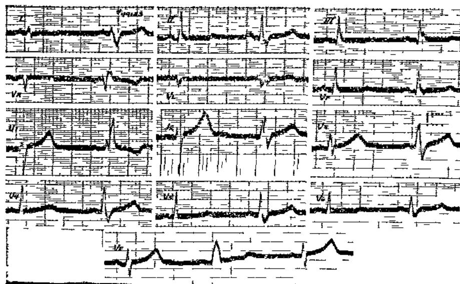


FIG 4 Partial right bundle branch block The first cycle of each pair represents normal intraventricular conduction the second represents complete right bundle branch block Lead V is small and lead V resembles leads V and V the heart is in a semi vertical position The standard leads show right bundle branch block of the less common or classical type when it is present This man aged 39 years had no other clinical signs or symptoms of heart disease Transient bundle branch block had been discovered four years earlier during a routine examination (From an article by Wilson Rosenbaum and Johnston)

cavity The S deflection results from the spread of the impulse through the free wall of the left ventricle and the final R wave is produced by the late activation of the free wall of the right ventricle and the right half of the septum toward the exploring electrode In lead V_1 the intrinsic deflection begins with the peak of the final R wave This peak has been found to occur at 0 10 to 0 12 sec after the beginning of the QRS complex On the other hand the intrinsic deflection in leads V and V_6

* This term is used to indicate that the peak of the deflection in question does not descend below or rise above the level of the trace at the beginning of the QRS interval

occurs at about 0 036 sec, just as when normal conduction is present The late intrinsic deflection over the right precordium and the normal intrinsic deflection over the left precordium confirm the belief that in right bundle branch block the left ventricle is activated at the normal time but the right ventricle is activated considerably later than normally As the exploring electrode is moved from the parasternal areas to the left

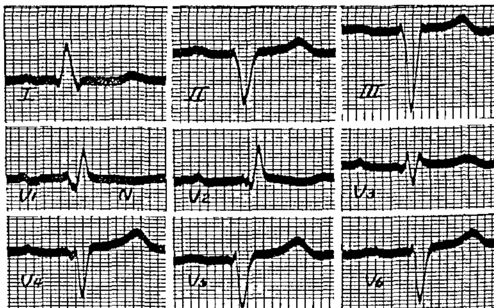


Fig 43 Right bundle branch block heart in the vertical position The standard leads show inconspicuous S waves in lead I and large broad S deflections in leads II and III Lead V shows the rsR configuration characteristic of right bundle branch block The small R deflections in leads V and V are unusual This man aged 62 had arteriosclerotic heart disease (From an article by F N Wilson[100])

precordium the small initial R wave grows rapidly larger and finally in leads V and V_6 it becomes a tall thin R spike occasionally preceded by a tiny Q wave On the other hand the larger R wave grows rapidly smaller becoming first a notch on the descending limb of the R wave and finally it is submerged in the broad rather shallow S deflection The transitional zone is placed well to the right usually recorded in leads V_3 or V but occasionally it may be to the right or left of these points or extend over a very wide area

An example of partial right bundle branch block is shown in Fig 4 This man, aged 39 had no other evidence of heart disease Transient

right bundle branch block was discovered four years earlier in the course of a complete physical examination Observations made one year after the records shown here disclosed persistent right bundle branch block In these records each lead is represented by two complete cardiac cycles Normal intraventricular conduction is present during the first and right bundle branch block during the second of each pair of beats These records illustrate the characteristic changes in the standard and unipolar limb leads and the multiple precordial leads in right bundle branch block with the heart in a semi vertical position Furthermore comparison of the block with normal records in the same patient is made very simple With the onset of right bundle branch block the QRS interval increases from 0 08 sec to 0 1- sec prominent slurred S waves appear in leads I and II the descending limb of the R wave in lead III becomes slurred and the T waves show minor changes The most striking change is seen in lead V_1 in this record the small initial R wave is preserved but the S deflection becomes embryonic and a large late R wave appears for the first time The R deflection is much smaller in lead V and in the remaining leads over the left precordium it is submerged in a broad slurred S wave In leads V_4 V and V the initial portions of the QRS complexes are much the same before and after the bundle branch block but the distinguishing feature is the development of a broad slurred rather shallow S wave Lead V_F shows a broad rather flat topped R wave rather than the distinctly bifid QRS complex seen in lead V_1 Such initial ventricular complexes occasionally occur in lead V_1 in right bundle branch block and are very similar to those recorded over the left precordium in left bundle branch block In the precordial electrocardiograms illustrated here the transitional zone corresponds to lead V with both normal and abnormal intraventricular conduction Lead V_F develops a prominent late R wave when right bundle branch block occurs whereas lead V_F resembles leads V and V and lead V_1 1 small the heart is therefore in the semi vertical position Electrocardiographic abnormalities such as these which indicate right bundle branch block at one instant and normal intraventricular conduction less than one second later cannot be attributed to some general change in the structure of the heart or one of its chambers Such phenomena can be explained only by assigning a critical function to a small zone or strand of tissue and they constitute a strong argument for the functional existence of the bundle branches in humans

An instance of right bundle branch block in which there are several unusual features is shown in Fig 43 These records are from a man aged

6 who had arteriosclerotic heart disease The standard leads display unusually large S deflections in leads II and III as well as other features which suggest left bundle branch block Close inspection discloses small Q and S waves in lead I these occur very rarely in left branch block but are quite common in right branch block These standard leads are quite similar to those shown in Fig 41c The electrocardiograms from the right precordium indicate that the delay in conduction involved the right ventricle because as in the more typical cases just described leads V_1 and V show large late R deflections Just as in the previous case this R deflection becomes progressively smaller and then disappears into the S wave as the electrode is moved to the left precordium However it is peculiar that the initial R wave fails to become increasingly taller as leads V and V are approached The reasons for this are not clear but there was probably an abnormality in the activation of the anterolateral aspect of the left ventricle The unipolar limb leads were not recorded in this patient but they can be estimated from the standard leads in the manner described by Wilson[1] Such an analysis indicates that the potential variations of the left leg were like those of the left precordium and those of the left arm like those of the right precordium Thus the heart was in a vertical position This unusual position undoubtedly was responsible for the unexpected outline of the standard leads in this case

When the QRS interval is 0 10 sec or longer in duration but less than 0 12 sec the electrocardiographic diagnosis of incomplete bundle branch block often can be made This is more apt to be possible in incomplete block of the right than of the left branch of the His bundle and in fact the later diagnosis usually is possible only under special circumstances It is usually necessary to take multiple precordial leads in order to diagnose incomplete bundle branch block and many instances will escape recognition unless such observations are made In many cases it is difficult to distinguish the changes produced by right ventricular hypertrophy from those of right bundle branch block and the two frequently coexist

The standard and unipolar limb leads in the lowest set of records in Fig 41 are those of a man age 40 who had rheumatic heart disease with calcific mitral stenosis and aortic insufficiency Nineteen months after these records were made he had a cerebral embolus from which he recovered with residual left hemiparesis The QRS interval in these records is 0 10 sec Prominent S waves are present in all of the standard leads and lead V_F A late broad R deflection is present in lead V_1 The precordial leads showed distinct late R waves in leads V_1 V and V_F This finding suggested delayed activation of the right ventricle Although incomplete

right bundle branch block was probably present associated right ventricular hypertrophy produced by the mitral stenosis probably played some part in producing the changes recorded

A situation which illustrates incomplete right bundle branch block more clearly and in which the diagnosis can be made with greater precision is shown in Figs 44 and 45 These records are from a man aged 65 who had arteriosclerotic heart disease and benign prostatic hyper

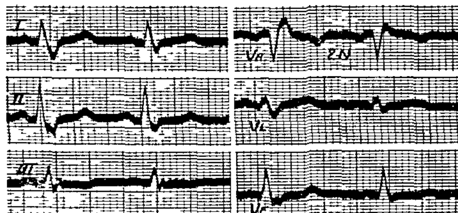


Fig 44 Complete and incomplete right bundle branch block standard and unipolar limb leads The first complex of each pair represents complete the second incomplete right branch block This patient aged 65 had arteriosclerotic heart disease (From an article by Wilson and associates)

trophy His blood pressure was 140/76 mm Hg and the physical examination disclosed an apical presystolic gallop rhythm In these records the first ventricular complex of each pair represents complete and the second incomplete right bundle branch block When the block is complete the characteristic changes are seen including the broad slurred S waves in leads I II V_L V_5 and V_6 the prominent slurred R deflection in lead V_R and the late R peak in leads V_1 and V This latter feature also occurs in additional records taken over the ensiform process and in the right mid clavicular line When the block becomes incomplete the QRS interval shortens from 0 14 sec to 0 11 sec The initial components of the QRS complexes in all leads remain identical This is true because they have their origin in the septum and the free wall of the left ventricle parts of the heart which are unaffected by the degree of delay in activation of the right ventricle However the later components

of the QRS complexes are altered in all leads the final S deflection is narrower and sharper in those leads where it was previously broad and the final R deflection in leads over the right precordium becomes much less conspicuous and is succeeded in many instances by a final S wave These differences no doubt are due to the fact that in incomplete right

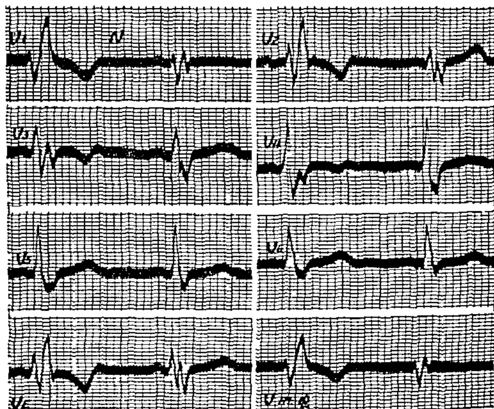


Fig 45 Complete and incomplete right bundle branch block precordial leads The first complex of each pair represents complete block the second incomplete right branch block The initial portion of the QRS complex has exactly the same outline in both Limb leads shown in Fig 44 (From an article by Wilson and associates[9])

bundle branch block the delay in activation of the free wall of the right ventricle is not as great as when the block is complete

The diagnosis of incomplete right bundle branch block presents many difficulties but when the standard leads show a QRS interval which is 0 09 to 0 11 sec in duration and a prominent S wave is present in lead I multiple precordial leads should be taken If such records reveal late R

deflections in leads V 1 and V (and usually V E) in addition to an initial small R peal incomplete right bundle branch bloc] usually may be said to be present

Left Bundle Branch Block

When the continuity of the left branch of the His bundle is interrupted the supraventricular impulse reaches the ventricles through the right bundle branch (Fig 40) The activation wave passes first through the septum all of which is activated in a right to left direction This manner of activation of the septum makes the right ventricle initially negative and the left ventricle initially positive The next stage is the excitation of the free wall of the right ventricle from within outward which makes both of the ventricular cavities negative Finally as the last stage in the depolarization of the ventricular myocardium the free wall of the left ventricle is activated from within outward this also produces negativity of both ventricular cavities If an exploring electrode is placed over the lateral wall of the right ventricle in a dog in whom left bundle branch block has been produced the QRS complex consists of a tiny initial R wave produced by activation of the relatively thin walled right ventricle followed by a deep S deflection produced by the later activation of the free wall of the left ventricle in a direction away from the point being studied The peak of the tiny R wave represents the onset of the intrinsic deflection it occurs early in the QRS interval and at the same time as when normal intraventricular conduction is present Furthermore leads from the right precordium show QRS complexes of this form in both experimental and human left bundle branch block[8] An electrode placed upon the epicardial surface of the free wall of the left ventricle in an animal with left bundle branch block records QRS complexes which consist of broad notched or bifid slurred R waves The initial upward movement of the trace is due to the activation of all the septum toward the electrode The activation of the free wall of the right ventricle produces a notch or dip at the peak of the R wave and the excitation of the lateral wall of the left ventricle is responsible for the final upstroke This final peak with its downward movement to the baseline represents the intrinsic deflection at this point over the heart It occurs very late in the QRS interval and this together with the absence of any S waves confirms the belief that this portion of the heart is the last to be activated Initial ventricular complexes of this form occur

in leads from the left precordium (leads V_5 and V_6) in both man and dogs with left bundle branch block[9]

The standard leads usually show several distinguishing features in this disorder The QRS interval is 0 12 sec or longer in duration The chief deflection in lead I is upright broad or flat-topped bifid or notched and slurred Except in rare instances no S or Q wave is seen in lead I and when the latter do occur in left bundle branch block it usually means that myocardial infarction involving the interventricular septum is also present[9, 101] The T waves usually are oppositely directed from the main deflection of the QRS complexes but the electrocardiographic diagnosis of either right or left bundle branch block is never dependent upon the form or direction of the final ventricular deflection The standard leads usually are discordant that is the main deflection of the QRS complex is upward in lead I and downward in lead III Less commonly the standard leads are concordant that is the major deflection of the QRS complexes is upward in both leads I and III Left bundle branch block may be accompanied by small bizarre QRS complexes or prominent S waves in lead I but such cases are exceedingly rare and the diagnosis then rests upon the character of the precordial electrocardiogram There is little that is characteristic about the unipolar limb leads in this condition Lead V_F usually shows large broad QS waves and the outline of leads V_L and V_F is dependent upon the electrocardiographic position of the heart These leads do give much useful information in understanding the variations which occur from case to case in the standard leads

Illustrations of the various types of left bundle branch block as they occur in the standard leads are shown in Fig 46 The precordial electrocardiograms of the upper three cases were characteristic of left bundle branch block The electrocardiograms in the upper row are those of a man aged 58 who had atypical angina pectoris and probable aortic stenosis In these records the QRS interval is 0 16 sec The QRS complex in lead I consists of a large slurred R wave The major deflections of the initial ventricular complexes are positive in lead I and negative in lead III therefore this may be designated as discordant left bundle branch block the most common form of this disorder Lead V_L shows complexes such as are recorded over the left precordium in this condition and lead V_F displays complexes such as are recorded from the right precordium The heart was in the transverse position It will be noted that in lead I and to a lesser degree in lead V_L the point at which the QRS complex terminates and the T wave begins the RS-T junction and segment is

displaced downward below the iso electric level This type of displacement of the RS T segment is more or less permanent and must be distinguished from the more transient displacements of this portion of the electrocardiogram which occur with angina pectoris or acute myocardial

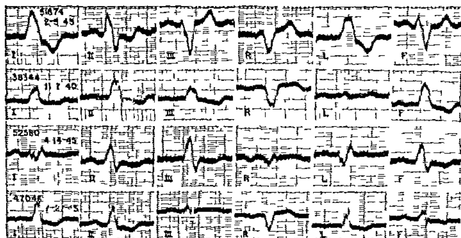


FIG 46 Various types of left bundle branch block Upper row left bundle branch block of the common type with large broad R waves in lead I and broad notched S deflections in lead III this is the classical discordant type Lead V_L resembles lead V and lead V_F resembles lead V_1 in this patient the heart was in the horizontal position This patient aged 58 had atypical angina pectoris and aortic stenosis Second row left bundle branch block of the less common type with broad flat topped R waves in all leads Lead V_L is small and lead V resembles lead V the heart was in the semi vertical position Note that lead V_F in this patient resembles lead V in the first case This man aged 69 had arteriosclerotic heart disease Third row left bundle branch block of the least common type Lead I shows a broad bizarre QRS complex with a conspicuous S deflection Q or S deflections in lead I are very rare in this disorder This man aged 33 had malignant hypertension he died four months after the records were made The precordial electrocardiograms in these three cases were identical in all major respects Fourth row incomplete left bundle branch block (See Fig 50)

infarction This particular type of displacement results when the T wave begins to be written before the QRS complex is completed and means that the recovery process has begun in some parts of the ventricular muscle before the activation process is completed in other areas

The electrocardiograms in the second row of Fig 46 are those of a man aged 69 who had arteriosclerotic heart disease They illustrate the concordant type of left bundle branch block which is encountered

much less commonly than that type just described The QRS interval is 0 13 sec long and broad flat-topped R waves are present in all of the standard leads In this case lead V_1 shows QRS complexes such as occur over the left precordium in this condition and lead V_L is small and bizarre the heart thus is in the semi vertical position The underlying defect in this case and in that illustrated in the upper record was the same The differences in the outline of the standard leads are due to the differences in the electrocardiographic position of the heart This is confirmed by the great similarity of lead V_1 in the first case and lead V_1 in the second The precordial electrocardiograms in the two cases were practically identical

The records in the third row of Fig 46 illustrate a rare type of left bundle branch block This man was 33 years old He had progressive hypertension for six years and was only temporarily relieved by a splanchnicectomy done six days before these records were made He died four months later, the post mortem examination disclosed tremendous cardiac hypertrophy coronary atherosclerosis and a recent myocardial infarction Lead I shows a small bizarre QRS complex with a conspicuous notched S wave The other standard leads show no distinctive features The unipolar limb leads indicate that the heart was in an indeterminate position The standard leads are actually somewhat more suggestive of right than left bundle branch block but the precordial leads were characteristic of the latter The records in the lowest row in Fig 46 illustrate a probable case of incomplete left bundle branch block This case is shown here in order that it may be contrasted with the examples of complete left branch block and will be discussed in detail later

Electrocardiograms taken from the right precordium (leads V_1 and V_2) in left bundle branch block show tiny R waves and deep broad S deflections or merely deep broad QS waves This negativity throughout all or nearly all of the QRS interval results from activation of first the interventricular septum and then the free wall of the left ventricle away from the exploring electrode The tiny initial R wave is produced by excitation of the free wall of the right ventricle but this positivity may be overbalanced by the spread of the impulse in the septum The intrinsic deflection in leads V_1 and V_2 occurs at 0 015 to 0 019 sec the normal time at these points Records taken from the left precordium (leads V_5 and V_6) show large broad notched or slurred R waves No Q or S deflections are recorded if the exploring electrode has been moved

beyond the transitional zone The positivity recorded throughout the QRS interval is due first to the activation of the septum and finally to that of the free wall of the left ventricle both toward the exploring electrode The excitation of the right ventricular wall is represented by a notch or dip at the peak of the R wave The intrinsic deflection begins with the final downstroke of the R wave it usually occurs 0 088 to 0 10 sec after the beginning of the QRS interval much later than the normal time of 0 036 sec

If the two ventricles were of the same thickness lead V_1 in right bundle branch block and lead V_6 in left bundle branch block would look alike similarly lead V_6 in right and lead V_1 in left branch block would appear the same They fail to do so primarily because the left ventricle is thick walled and the right ventricle is thin walled Generally speaking it may be said that in left bundle branch block the QRS complexes in leads V_1 and V_6 are monophasic whereas in right branch block corresponding records are diphasic or triphasic In left branch block the transitional zone is displaced to the left It usually occurs in lead V_4 but occasionally may correspond to leads V and V_6 In such cases it may be necessary to take records in the left anterior axillary line or left scapular line to obtain the large broad R waves which represent the typical potential variations of the left ventricular surface in this condition

The electrocardiograms in Fig 47 are those of a man aged 65 who had rheumatic heart disease and angina pectoris A post mortem examination made six months after the observations shown revealed aortic and *mitral stenosis a small infarct of the interventricular septum and another* in the posterior wall of the left ventricle These tracings show transient left bundle branch block In the records made on January 7 1941 the QRS interval measures 0 16 sec and the standard leads are characteristic of discordant left bundle branch block No Q or S deflections are seen in leads I or V_L Three days later the QRS interval has shortened to 0 10 sec there is marked left axis deviation and the standard leads are characteristic of left ventricular hypertrophy with associated myocardial changes The precordial leads were taken with the sensitivity of the string reduced to one half normal (0 5 cm = 1 mv) When left bundle branch block is present lead V_1 shows large QS deflections leads V and V_3 show tiny R waves and broad S waves and leads V_5 and V show broad slurred or notched R deflections with no Q or S waves When normal conduction is present the QRS complexes over the right

precordium are not so different except that the QRS interval is shorter, but over the left precordium the R waves become taller more slender and sharply peaked The configuration of the QRS complexes in leads

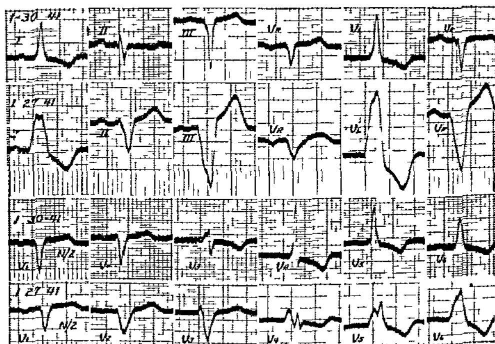


Fig 47 Transient left bundle branch block heart in the horizontal position January 27 1941 discordant left bundle branch block The QRS interval measures 0 16 seconds and the QRS complexes of leads I V V and V consist of broad notched R waves The large QS deflections in leads V and V are also characteristic of this condition January 30 1941 normal intraventricular conduction The standard leads show left axis deviation with inverted T waves in leads I and II The precordial leads show inconspicuous R waves and large S deflections over the right precordium and tall R waves with inverted T waves in leads V V and V These are the electrocardiographic signs produced by left ventricular hypertrophy with associated myocardial changes Precordial leads taken with the galvanometer at one half normal sensitivity reducing the size of the deflections by one half In both sets of records lead V_F resembles leads V and V and lead V resembles V the heart was in the horizontal position This man aged 65 died six months later He had aortic and mitral stenosis and infarcts of the interventricular septum and the posterior wall of the left ventricle

V_5 and V_6 as seen here during left bundle branch block together with the late intrinsic deflection in these leads is the most distinguishing electrocardiographic feature of this condition The transitional zone

corresponds to lead V_4 in this case when the block is present and it shifts to lead V_3 when intraventricular conduction becomes normal On

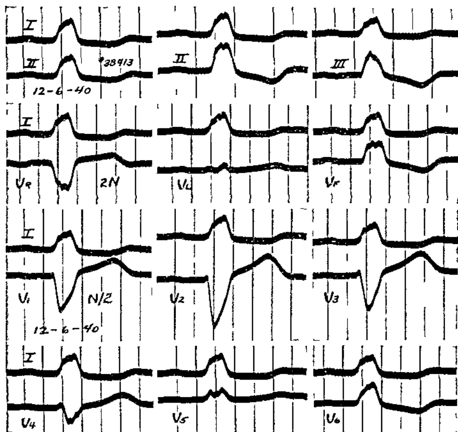


Fig 48 Left bundle branch block heart in the semivertical position The upper record in each instance is lead I recorded simultaneously The initial ventricular complexes of the standard leads consist solely of a broad slurred R wave The precordial leads recorded at one half normal sensitivity show tiny or absent R waves and broad slurred S deflections in leads V V and V and broad flat topped R waves in lead V Lead V is small and lead V resembles lead V the heart is in the semivertical position This man aged o had arteriosclerotic heart disease at other times the standard leads were of the more common type but the precordial leads were unchanged (From an article by Wil on and associates)

the whole it is seen that the T waves are directed oppositely to the major deflections of the QRS complexes Furthermore the T waves become

more inverted in leads I V_L and V_6 when left branch block is present and producing bigger, broader R waves in those leads This more striking change in the T waves is dependent upon the change in the QRS complexes associated with the intraventricular block and not upon a change in the heart as a whole The unipolar limb leads indicate that the heart is in the transverse position This is the most common electrocardiographic position in left bundle branch block because the patients who have the type of heart disease which is associated with this disorder also usually have left ventricular hypertrophy arteriosclerosis of the ascending and transverse aorta or are obese, all factors which make for a transverse position of the heart

The precordial electrocardiograms in a patient with concordant left bundle branch block are illustrated in Fig 48 Standard leads recorded from the same patient a few days earlier are shown in Fig 46b Eight months earlier his electrocardiograms showed left bundle branch block of the more common type At all times the precordial leads were characteristic of left bundle branch block Leads from the right precordium show tiny or absent R waves and large broad S deflections Records from the left precordium display broad slurred R waves with no Q or S deflections The transitional zone is between the fourth (V_4) and fifth (V) precordial points explored The precordial electrocardiogram in this case was practically identical with that of the patient whose records are shown in Fig 47 The standard leads are different because the heart was placed semivertically in this case and horizontally in the other man

The patient whose electrocardiograms are reproduced in Fig 49 was a 56-year old man who had hypertensive heart disease Many observations were made over a period of one month The standard leads were quite variable in outline but the precordial electrocardiograms were always characteristic of left bundle branch block The standard leads taken on February 28 1941 display broad S waves in lead I and tall R deflections in lead III suggesting right bundle branch block The records taken on March 14 show small bizarre QRS complexes in lead I and tall R waves in leads II and III these records resemble those of Fig 46c Study of the unipolar limb leads together with the precordial leads indicates that *when the first observations were made the heart was* in the vertical position since the potential variations of the left arm resemble those of the right precordium and those of the left leg are like those of the left precordium On the later date the potential variations of the left arm and leg were quite different and the heart was apparently

in a somewhat different position The underlying defect and the precordial electrocardiogram remained constant in this case but the configuration of the standard leads alone in cases such as this may lead to erroneous electrocardiographic diagnoses When in cases of left bundle branch block the potential variations of the right ventricle are transmitted to the left arm and those of the left ventricle are transmitted to the left that is when the heart is vertically placed it is difficult to distinguish right from left bundle branch block from the standard leads alone and multiple precordial leads must be taken to arrive at the correct conclusion

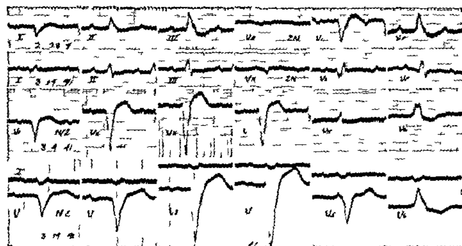


Fig 49 Left bundle branch block heart in the vertical position February 28 1941 the standard leads show broad slurred S waves in lead I and prominent notched R waves in lead III These changes suggest right branch block The precordial leads in March 4, 1941 however are typical of left bundle branch block Lead V_2 resembles lead V and lead V resembles lead V_6 indicating a vertical position of the heart March 14 1941 the limb leads now show small bizarre QRS complexes in all leads indicating a shift in the position of the heart but the precordial leads are again characteristic of this disorder This man aged 6 had hypertensive heart disease with congestive failure (From an article by F N Wilson)

Incomplete left bundle branch block usually is difficult to diagnose with certainty because the records resemble those of left ventricular hypertrophy and the two conditions frequently coexist The presence of Q waves in leads I V and V_6 usually excludes the possibility of incomplete left branch block but the absence of Q in these leads does not

differentiate it from left ventricular hypertrophy A probable example of this condition in a man aged 54 with arteriosclerotic heart disease is shown in Figs 46d and 50 The QRS interval is 0 10 to 0 11 sec in duration and in general configuration the curves are much like those of

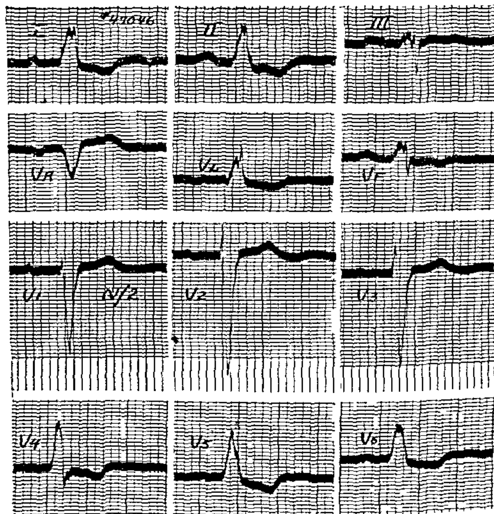


Fig 50 Incomplete left bundle branch block heart in the semi horizontal position The QRS interval measures 0 10 seconds The QRS complexes in leads I V and V consist of broad flat topped or notched R waves Except for the duration of the QRS interval these records are very similar to those of complete left branch block. Lead V_L resembles lead V_6, and the area of QRS in lead V_F is small the heart is in the semi horizontal position These records are from a man aged 54 with arteriosclerotic heart disease

the examples of complete left branch block already illustrated The peaks of the R waves in leads I V_5 and V_6 are notched or slurred and not tall and peaked as they are in left ventricular hypertrophy, no Q or S deflections occur in these leads The unipolar limb leads indicate that the heart is in a semi horizontal position

Electrocardiograms are encountered occasionally which show a QRS interval measuring 0 1 sec or more and yet the records do not resemble those which we classify as right or left bundle branch block Such tracings usually display small broad notched QRS complexes in all leads They probably represent some delay in the activation of local regions of muscle or a focal block at the finer arborizations of the Purkinje network[10] Records of this type are seen most often in patients who have had numerous myocardial infarctions or who have a generalized functional depression or actual degeneration of the myocardium due to some toxemia such as uremia or to some drug such as quinidine Many cases which previously would have been classified as arborization block from the standard leads now are diagnosed more correctly as right or left bundle branch block because the precordial electrocardiogram is characteristic of one or the other of these conditions

Bundle branch block occurs in a large number of cardiac disorders It is most common in arteriosclerotic and hypertensive heart disease[103] It may complicate myocardial infarction and when it does the prognosis is more grave[67] although the conduction defect often proves transient Intraventricular block may be present in congenital heart disease particularly if there is a defect in the interventricular *or interauricular* septum I have observed several examples of incomplete right bundle branch block indicated primarily by the precordial electrocardiogram in children with Roger s disease Transient right bundle branch block may occur in pulmonary embolism[101] and Rotta observed persistent conduction defects of this type in 7 per cent of men living at high altitudes in the Andes[10] Quinidine has been reported to produce right bundle branch block[40] and I have seen a young woman with mitral stenosis and auricular flutter who developed transient left bundle branch block when given that drug When rheumatic heart disease with mitral stenosis is complicated by a conduction defect the lesion usually is on the right[103] but the writer has seen a case with classical left bundle branch block Syphilitic heart disease also may be associated with intraventricular block particularly if a gumma involves one of the bundle branches Not infrequently young or middle aged individuals are discovered to have bundle branch block quite accidentally when routine examinations are

done Such cases may have no cardiac symptoms whatever The abnormality may well represent an old scar or some minor congenital anomaly of the conduction system

The significance of bundle branch block is merely that it points to some myocardial change which has involved the specialized conduction tissue In this situation the electrocardiogram furnishes information which is available in no other way However the electrocardiographic change may be produced either by widespread degenerative change which has involved the specialized tissues as well as the ordinary cardiac muscle or it may be produced by a single isolated lesion in a strategic location Therefore the electrocardiograms must be evaluated together with the entire clinical picture If the intraventricular block is due to some recent active process it has great significance, if it represents an old healed lesion it has relatively little importance At one time it was held that bundle branch block indicated an average life expectancy of two to three years such prognoses must rest upon the underlying heart disease and not upon the electrocardiographic abnormality alone Right bundle branch block has been said to be more common and to carry a better prognosis than left branch block[10a] This may be true because the length of the undivided portion of the bundle branch is greater on the right than on the left making it more likely to be involved by and more susceptible to single isolated lesions It has been maintained that the clinical diagnosis of bundle branch block can be made upon finding a split first sound and a double systolic impulse at the cardiac apex produced by ventricular asynchronism Although ventricular asynchronism does exist in this disorder[8] it has been shown that the split apical sound actually is due oftentimes to a presystolic gallop and therefore cannot be due to asynchronous ventricular systole at all[10]

Ventricular Hypertrophy

The electrocardiogram often displays certain characteristics which make it possible to localize predominant hypertrophy to one of the ventricles Although this diagnosis usually can be predicted from the clinical picture and radiographic examination in certain circumstances the electrocardiogram may have considerable diagnostic importance Electrocardiographic evidence pointing to either right or left ventricular hypertrophy may be of help in the differentiation of various types of congenital heart disease For example one of the most important features differ-

entiating tricuspid atresia from the tetralogy of Fallot is that in the former the standard leads show left axis deviation and the precordial electrocardiogram is suggestive of left ventricular hypertrophy whereas in the latter the limb leads display right axis deviation and the precordial leads suggest right ventricular hypertrophy The electrocardiographic signs of left ventricular hypertrophy may point to antecedent hypertension in a patient whose blood pressure is normal when seen first because of an acute febrile illness or some other acute process which reduces the blood pressure temporarily Evidence of right ventricular hypertrophy may call attention to mitral stenosis or left ventricular hypertrophy may point to aortic stenosis or insufficiency either of which occasionally may escape the examining physician The changes in the electrocardiogram which indicate ventricular hypertrophy are primarily in (a) the mean electrical axis (b) the axis deviation index and (c) the configuration of the precordial electrocardiogram

Mean Electrical Axis

It has been mentioned that Einthoven suggested that the heart may be considered to be at the center of a sphere and the attachments of the three extremities may be looked upon as the apices of an equilateral triangle with these points at the surface of the sphere Furthermore the plane of this triangle corresponds to the frontal plane of the body and passes through the center of the sphere The sides of the triangle are thus formed by lead I (LA − RA) lead II (LL − RA) and lead III (LL − LA) The electromotive force developed by the heart at any instant can be represented by a vector which like all vector quantities has both magnitude and direction The projection of this vector upon the three sides of the triangle gives the size and direction of the deflection which the force produces at that instant in each of the standard leads

The average direction which this vector takes throughout the QRS interval in relation to the line of lead I (the LA RA side of the triangle) is designated the mean electrical axis That is the average of all the instantaneous axes throughout the QRS cycle is the mean electrical axis The angle which the electrical axis makes with the line of lead I is called α A force which is parallel to lead I and directed from the right arm toward the left arm is said to have an electrical axis of 0 Forces above the line of lead I are represented as minus and forces below this line are represented as plus The range of values for the angle α of normal

patients is between 0° and +90°. When the mean electrical axis is outside this range, axis deviation is said to be present. A sharp line cannot be drawn between normal and abnormal electrocardiograms in this respect, and rarely normal individuals will be seen whose mean electrical axes range up to minus 30° or to plus 110° or plus 115°.

When the axis is rotated counterclockwise, in the minus direction, that is above the line of lead I so that the angle α is less than 0°, usually minus 30°, minus 60° or minus 90°, the diagnosis of left axis deviation is made. This change is almost always associated with left ventricular hypertrophy. When the axis is rotated clockwise, in the plus direction, beyond a line perpendicular to lead I so that the angle α is more than plus 90°, usually plus 120°, plus 150° or plus 180°, right axis deviation is the diagnosis. This usually indicates right ventricular hypertrophy.

The mean electrical axis is determined from the areas of the QRS complexes in any two of the standard leads, usually leads I and III. The term *area* is used here to mean the algebraic sum of those portions of the curve which lie between the bottom of the trace and the isoelectric line for each of the components of the QRS complex. Accurate measurements of the electrical axis are cumbersome and time consuming. Techniques such as the charts of Carter, Richter and Greene[108] and Dieuaide[109] and the triaxial reference system of Bayley[110] usually are satisfactory, although they are subject to the criticism that the amplitude of the deflections usually is used instead of the actual areas. For all practical purposes the mean electrical axis can be estimated to the nearest 30° by simple inspection of the standard leads, keeping in mind the Einthoven triangle and some such system of electrocardiographic patterns as that illustrated in Fig. 51[111]. This method is applicable except in those cases in which the net area of QRS is very small in all leads. Two principles are of help when this system is used: (a) when the direction of the mean electrical axis is perpendicular to the line of one of the standard leads, the QRS complex is isoelectric in that lead only, i.e., the positive and negative areas are equal so the net area is zero; (b) when the axis is parallel to the line of one of the standard leads, the deflections are larger and the net area is twice as large in that lead as in either of the other two. For many practical purposes the electrocardiographic area of the ventricular complexes can be estimated by the technique described by Ashman and Byer[11].

The axis deviates in one or the other direction in ventricular hypertrophy because usually the number of muscle units or the mass of muscle activated in that direction is increased. In *left ventricular hyper*

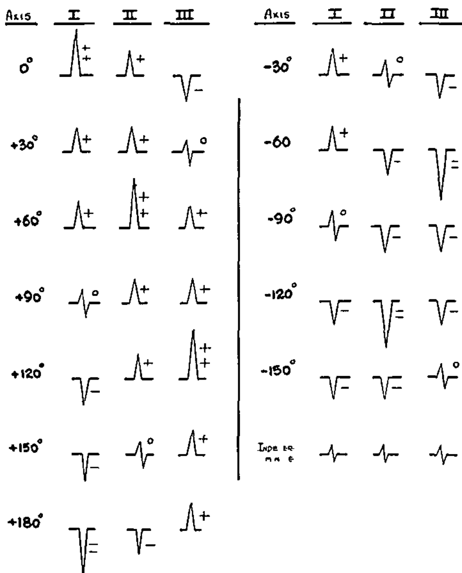


Fig 51 Diagrams illustrating the various possible patterns of the standard leads and the corresponding mean electrical axes An electrocardiographic area which is positive is designated + if it is negative it is labelled − If it is also large it is designated as ‡ or = The sum of the designations of leads I and III always should equal that of lead II

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The axis deviates in one or the other direction in ventricular hypertrophy because usually the number of muscle units or the mass of muscle activated in that direction is increased. *In left ventricular hyper-*

hypertrophy The index is influenced considerably by the size of the deflections In left ventricular hypertrophy large deflections are common and indices above plus 20 are almost always abnormal Patients with right ventricular hypertrophy especially with mitral stenosis often have records showing small deflections so that indices of −10 or less are not uncommon and this particular indication of the hypertrophy may be absent

Relative Significance of Mean Electrical Axis and Axis Deviation Index

It is well to determine both the mean electrical axis and the axis deviation index in most cases As a sign of ventricular hypertrophy the former probably is more often faulty If the mean electrical axis is abnormal and the index is within the normal range the curve is not necessarily abnormal Left axis deviation often is associated with inverted T waves in lead I and right axis deviation with inverted T waves in leads II and III Such electrocardiograms are clearly abnormal and the significance of the axis deviation in such cases usually is evident If the axis deviation index is abnormal and the mean electrical axis is normal the tracing is probably an abnormal one The index is more apt to fail to indicate right than left ventricular hypertrophy Occasionally both of these measurements may fail especially when the heart is in an unusually vertical position (Fig 54) Lewis[115] and later Herrmann and Wilson[116] made attempts to correlate the electrocardiographic signs with the type of hypertrophy found at post mortem On the whole good agreement was found when the heart was greatly hypertrophied but puzzling discrepancies were encountered when the heart was normal in size or only slightly enlarged These studies indicated that factors which modify the influence of the relative ventricular weights upon the form of the ventricular complex include intraventricular conduction defects and the position of the heart The mean electrical axis changes with advancing years progressing generally toward the left The average for the various ages have been given as (a) under 6 months plus 130 (b) 1 to 5 years plus 52 (c) puberty plus 67 (d) adult plus 58[117]

PRECORDIAL ELECTROCARDIOGRAM IN VENTRICULAR HYPERTROPHY

The position of the heart does not influence the configuration of the precordial electrocardiogram nearly so much as it does that of the limb

trophy the free wall of the left ventricle grows thicker thereby increasing the number of muscle units activated from right to left and upward Consequently the mean electrical axis rotates counter clockwise to the left and upward in this condition In *right ventricular hypertrophy* the lateral wall of the right ventricle thickens increasing the muscle activated from left to right and downward and causing the electrical axis to rotate in a clockwise direction The electrocardiographic diagnosis of left or right axis deviation has come to be associated with left or right ventricular hypertrophy respectively in the mind of the clinician Consequently it is the general practice to reserve the diagnosis of axis deviation for those situations in which the QRS complex is normal apart from the shift in the electrical axis It is true that the electrical axis in bundle branch block may be quite abnormal because all of the septum is activated in one direction thereby increasing the total mass of muscle being activated from right to left (left bundle branch block) or left to right (right bundle branch block) but usually the simultaneous diagnosis of axis deviation is not made because the ventricular hypertrophy implied thereby is not necessarily present No close correlation between the degree of axis deviation and the significance of the electrocardiogram has been established The mean electrical axis of the P or T waves can be determined also by measurement of the areas of those deflections in the standard leads

Axis Deviation Index

The axis deviation index is determined from the voltage of the R and S deflections in leads I and III The index is obtained by subtracting the sum of R_3 and S_1 from the sum of R_1 and S_3[114] If there is no S wave in either leads I or III but a Q deflection is present or if an S wave is present but a Q wave which is larger is also present in either of these leads then Q is substituted for S in the formula If unipolar limb leads are recorded a similar index is given by determining the algebraic sum of the positive and negative deflections of the QRS complex in lead V_1 and multiplying the result by 2[114] The average index determined by Wilson and Nyboer in a study of 104 normal young men was −2.68[114] The upper limit of normal in this index is plus 20 deviations beyond that limit suggest left ventricular hypertrophy The lower limit of normal is taken as −20 although experience suggests that −15 may be a more practical figure deviations below this level suggest right ventricular

The records in Fig 52 were taken from a man aged 37 who was discovered to have hypertension two years before the first observations were made At the initial examination the blood pressure was 245/145 mm Hg severe hypertensive retinopathy was present and the heart was

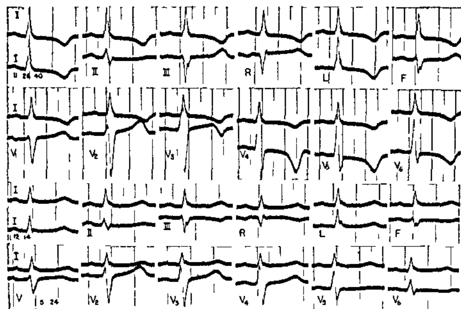


FIG 52 Left ventricular hypertrophy heart in the horizontal position November 26 1940 the standard leads show left axis deviation The mean electrical axis is minus 30 and the axis deviation index is plus 33 The precordial leads show relatively small R waves and large S waves in leads V and V_2 and large R deflections and inverted T waves in leads V V_5 and V_6 Note that lead V resembles V_R, whereas lead V is similar to lead V December 14 1944 the mean electrical axis is still minus 30 but the axis deviation index is only plus 15 The deflections are much smaller in all leads particularly over the precordium and the T waves are normal except in leads V and V where they are flat This man aged 38 had a blood pressure of 245/145 mm Hg at the time of the initial observations and a splanchnicectomy was done soon thereafter When the second set of records was made the blood pressure was 124/86 mm Hg (From an article by Wilson Rosenbaum and Johnston[7])

moderately enlarged A splanchnicectomy was done When he was examined four years later the blood pressure was 124/86 mm Hg only minor retinal arterial changes were found but he had developed mild angina pectoris The upper set of electrocardiograms taken in 1940 show the characteristic changes of left ventricular hypertrophy in an

leads The precordial electrocardiograms of normal individuals whose standard leads show mean electrical axes deviated to the right or left or lying in the normal range are all essentially the same Because this is true and because the precordial electrocardiogram shows distinctive changes in ventricular hypertrophy, precordial leads should be used whenever that diagnosis is being considered

The differences in the normal electrocardiograms recorded from the right and left precordium stem primarily from the greater thickness and bulk of the left ventricle as compared with that of the right chamber When *left ventricular hypertrophy* occurs this difference in relative thickness and bulk of the two chambers becomes exaggerated and consequently the precordial electrocardiogram shows an exaggeration of the normal differences in the records from the right and left precordium[9] The deflections particularly the chief deflection of the QRS complex tend to grow larger so that it may be necessary to reduce the sensitivity of the galvanometer to one-half normal (1 mv = 0 5 cm) in order to record all of the tracing on the recording paper In leads V_1 and V the R waves grow smaller or may even be absent the S waves become considerably larger and the time of the intrinsic deflection remains unchanged or becomes slightly earlier in the QRS interval The time of the intrinsic deflection over the right precordium is unchanged because the thickness of the right ventricle is unchanged and the time required for the activation wave to traverse the lateral wall of the right ventricle and arrive at the epicardial surface is normal Leads V_4, V_5 and V_6 display R waves which are considerably larger than normal and intrinsic deflections which are 0 02 to 0 03 sec later than normal The greater time required for the activation wave to traverse the thickened left ventricular wall and the resultant delay in arriving at the epicardium are believed to account for these changes Small Q waves appear in records from those points showing the largest R deflections probably because of earlier activation of the subendocardial muscle in other areas S deflections usually are small or absent over the left precordium The QRS interval tends to be lengthened it is usually 0 10 to 0 11 sec Occasionally it may measure 0 12 sec but intraventricular or focal block may be present in such cases The T waves often are inverted in leads V_4 V and V_6 and in these same records the RS T segment may show depression of the more permanent type which results from the onset of repolarization in some zone of the myocardium before depolarization is completed in all other areas The transitional zone usually is displaced to the left

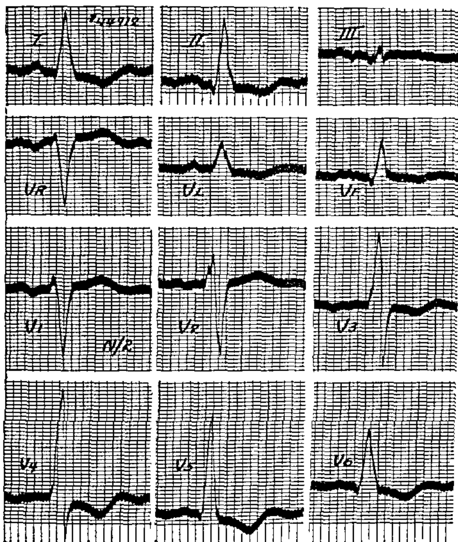


FIG 53 Left ventricular hypertr phy heart in the intermediate position The standard leads show broad slurred QRS comp le es and inverted T waves in all lead The mean electrical axis is plus 30 and the axis deviation index is plus 13 The precordial leads recorded at one half normal sensitivity are characteristic of left ventricular hypertrophy Leads VL and V are much alike and both resemble V this indicates an intermediate position of the heart which in turn accounts for the absence of the usual evidence of left ventricular hypertrophy in the standard leads These records are from a man aged 4 with malignant hyp rtensi n h s bl od pressure wa 26 /158 mm Hg

individual with the heart in a horizontal position. In the standard leads the mean electrical axis is −30 (the area of the QRS complex is zero in lead II, therefore the axis is perpendicular to the line of that lead), the axis deviation index is plus 33 and the T waves are distinctly inverted in lead I and slightly inverted in lead II. Leads V_1 and V_2 show small R waves and large S deflections; leads V_4, V_5 and V_6 display very large R waves, deeply inverted T waves and slight depression of RS-T segment. Lead V_L displays QRS complexes like those recorded from the left precordium and lead V_F resembles the records from the right precordium, indicating a transverse position of the heart. The second set of records made four years after the operation look quite different. The mean electrical axis is still −30 and the unipolar limb leads again indicate a horizontally placed heart but the axis deviation index is only plus 15 and the T waves are now upright in leads I, II and V_L. The precordial electrocardiogram is normal except for the unusually flat T waves in leads V_5 and V_6 and the peculiar shift of the transitional zone to the left. This reversion of the electrocardiogram to a more normal outline following surgical relief of hypertension has been reported by several observers.[118, 119] It probably results in part from the improved nutrition of the ventricular muscle and possibly to some regression of the ventricular hypertrophy.

Left Ventricular Hypertrophy

When left ventricular hypertrophy occurs in an individual whose heart is in the intermediate position the standard leads may fail to show the usual signs of this disorder. The man whose records are reproduced in Fig. 53 was aged 45. He had hypertension for two years. His blood pressure was 262/158 mm Hg when these studies were made. Severe impairment of the renal function contraindicated splanchnicectomy. The mean electrical axis is plus 30 (the QRS complex is small and isoelectric in lead III and the axis is, therefore, perpendicular to line of lead III) and the axis deviation index is plus 13. The broad, slurred QRS complexes in all leads and inverted T waves in leads I and II are the major abnormalities in the standard leads. The precordial curves display the characteristic changes of left ventricular hypertrophy. Even when recorded with the galvanometer at one half the normal sensitivity the chief deflections of the QRS complexes of the precordial leads are unusually large. The QRS interval is 0.11-0.12 sec in duration. Leads V_L

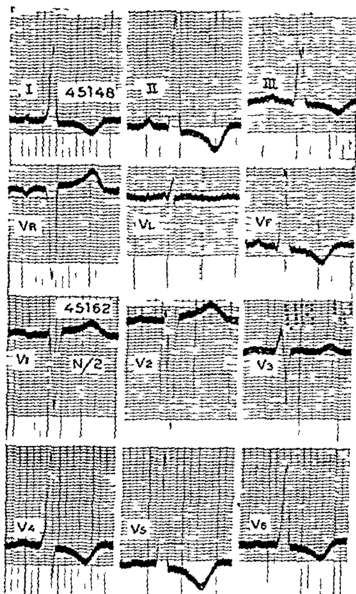


Fig 54 Left ventricular hypertrophy [illegible] heart [illegible] semi [illegible] position The standard leads [illegible] unusually tall R [illegible] in lead II [illegible] T waves in all leads The precordial leads [illegible] are typical of left ventricular hypertrophy [illegible] small [illegible] heart is in the semi [illegible] position [illegible]

and V_F are similar in outline and resemble lead V_6, the heart was in the intermediate position

The electrocardiograms illustrated in Fig 54 are those of a woman aged 50 years whose blood pressure was 220/120 mm Hg She had severe hypertensive retinopathy moderate cardiac enlargement, distinct reduction of the renal function and a history of paroxysmal nocturnal dyspnea She was only slightly improved by splanchnicectomy The standard leads show a mean electrical axis of plus 60° (the largest deflections are in lead II and the axis is therefore, parallel to line of that lead) and an axis deviation index of plus 6 Although these values are normal the R deflections are abnormally tall, particularly in lead II, the QRS interval is slightly increased and the T waves are inverted in all leads Experience has shown that standard leads of this configuration usually point to left ventricular hypertrophy in a patient whose heart is in the semi vertical position The precordial electrocardiograms are characteristic of left ventricular hypertrophy The tiny R waves and large S deflections in leads V_1 and V[illegible] and the tremendous R spikes, absent S waves and inverted T waves in leads V_5 and V_6 are quite typical of this condition Since the potential variations of the left leg resemble leads V[illegible] and V_6 and those of the left arm are small the heart is in the semi vertical position Because of this uncommon position of the heart the usual indices of ventricular hypertrophy were absent in the standard leads and the clinician who employed these signs alone in evaluating the electrocardiograms in this patient would have been led astray

The records shown in Fig 55 are those of a young man aged 16 years who had rheumatic heart disease with aortic stenosis and insufficiency and probably mitral stenosis The cardiac apex was found to be nearly in the posterior axillary line at the level of the seventh intercostal space The standard leads show right axis deviation with inverted T waves in leads II and III The mean electrical axis is plus 120 (the largest deflections are in lead III and the axis is therefore, parallel to line of lead III) and the axis deviation index is minus 26 These findings suggest right ventricular hypertrophy The precordial curves are quite typical of left ventricular hypertrophy The time of the intrinsic deflections was measured and the delay in leads V_6 and V_7 (left posterior axillary line at the level of the apex) is well shown No unipolar limb leads were recorded but they can be estimated from the standard leads Such derivations indicate that the potential variations of the left arm were like those of the right precordium and the potential variations of the left leg resembled those of the left precordium The heart was therefore in the

vertical position thereby accounting for the very unusual pattern of the standard leads

Right Ventricular Hypertrophy

When right ventricular hypertrophy occurs the normal difference in the thickness and bulk of the right and left ventricular walls tends to be diminished or even reversed. Consequently in advanced right ventricular hypertrophy there is a reversal of the normal pattern of the precordial electrocardiogram so that records from the right precordium resemble those which normally occur over the left chest and curves from the left precordium resemble those normally obtained from points to the right of the sternum[3]. In less advanced right ventricular hypertrophy the alterations in the precordial curves may not be so clear cut. As a rule in right ventricular hypertrophy the R waves in leads V1 and V2 become much taller and the time of the intrinsic deflection is changed from 0 01 sec to 0 03 or 0 05 sec. These changes reflect the greater time the activation wave requires to spread through the thickened right ventricular wall. Tiny Q waves often appear in leads V1 and V2 and in these leads the S deflections are very small or absent. The T waves usually are inverted in leads V1 and V2 and often in leads V3 and V4. Records from the left precordium show R deflections which are abnormally small and definitely smaller than those in lead V1, S waves which are unusually large and intrinsic deflections which occur at the normal time. There are no Q waves in leads V5 and V6 and the T waves usually are upright. The voltage of the chief deflections of the QRS complexes tends to increase but not nearly as much as in left ventricular hypertrophy. The QRS interval usually is not increased unless bundle branch block is present also. The transitional zone tends to be displaced to the right. This electrocardiographic pattern occurred in thirteen cases of a total of forty patients observed by Myers and his associates and proven to have preponderant right ventricular hypertrophy at autopsy.

The study of Myers and his co workers disclosed that in some patients with heart disease producing right ventricular hypertrophy it is necessary to take records farther to the right than the customary lead V1 position to obtain records displaying the characteristic large late R deflections small Q waves and inverted T waves which occur over the right precordium in this disorder. Incomplete or complete right bundle branch block occurs in other individuals with right ventricular hypertrophy; in such cases there is a double peaking of the R wave or a

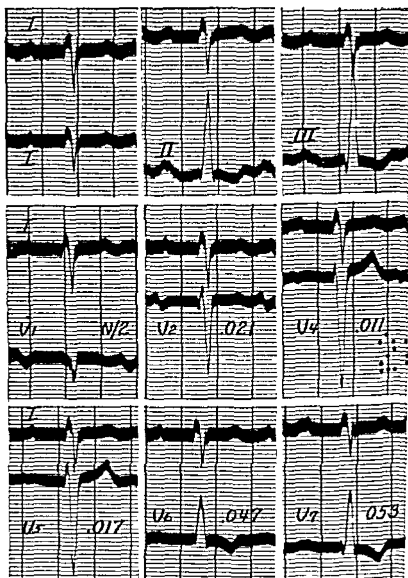


FIG 55 Left ventricular hypertrophy heart in the vertical position The standard leads show right axis deviation and inverted T waves in leads II and III The mean electrical axis is plus 120 and the axis deviation index is minus 6 These findings *suggest right ventricular hypertrophy but the precordial leads indicate* left ventricular hypertrophy An unusually vertical position of the heart is responsible for this apparent discrepancy Lead V was recorded from the left posterior axillary line at the level of the apex The upper curve in each record is lead I recorded simultaneously The time of occurrence of the intrinsic deflection is indicated in the precordial lead This young man aged 16 years had rheumatic heart disease with aortic stenosis and insufficiency and possibly mitral stenosis (From an article by Wilson and associates)

commonly seen in this disorder Lead V₂ resembles leads V and V₅ and lead V₁ resembles lead V₁ the heart was in the horizontal position

The lower set of electrocardiograms in Fig 56 are those of a man aged 40 who had rheumatic heart disease with mitral stenosis and aortic insufficiency The standard leads show small R waves and unusually

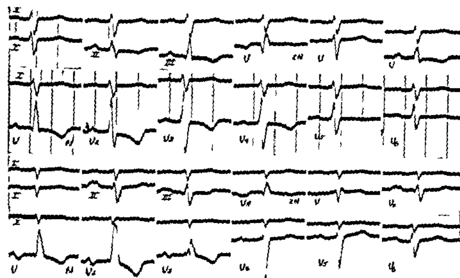


Fig 56 Right ventricular hypertrophy Upper t r c r l heart in the horizontal position The standard lea l h deh it r g l t l deviation m rred T waves in leads II and III a mean ele trical a t plu and an axi deviation index of minus 3 The precordial lea l ar typic l f right entricular hyp rtrophy with complete rever al c f the u ual pattern i e t ll R a e m l tm S v a es in lead V and small R waves and prominent S v a e l lead V Th man aged 34 had pulmonary hypertension probably lue t primary pulmonary vascular disease

Lower tw records heart in the conv ert cal p itn The standard l ads show small R wave and large S deflect n m all l a l a n n l t ral f n inu t o and an axis deviation index of minus 3 The pre ordial l ad are typ al of right ventricular hypertrophy and re nble th se f th first a e Sin lead V resembles lead V₄ and lead V t an ll th l eart the c n rt al p ation The man aged 40 had mitral stenosis and aortic insufficiency (From an article by Wilson and associates)

prominent S deflections in all leads The mean electrical axis is minus 150 (or plus 210) indicating a very unusual type and degree of rotation The axis deviation index is minus 3 The usual indices of right ventricular hypertrophy are not present in the limb leads yet the precordial leads are characteristic of that condition and show the same

prominent late R deflection in leads V_1 and V_2. Neither complete nor incomplete right bundle branch block can be considered pathognomonic of right ventricular hypertrophy, and when this disturbance of intraventricular conduction occurs it may be said to obscure the electrocardiographic diagnosis of right ventricular hypertrophy. Electrocardiographic changes of right ventricular hypertrophy failed to appear in the precordial and unipolar limb leads in seven of the forty cases in which that diagnosis was established at autopsy by Myers and associates.[10] The pattern of the electrocardiogram in right ventricular hypertrophy is the same irrespective of the exact nature of the underlying disease. Kossmann and his associates[11] have emphasized recently that there are several disorders other than right ventricular hypertrophy which may produce right axis deviation. These workers have questioned that the hypertrophied right ventricle by itself causes right axis deviation and have suggested that its dominant effect upon the electrocardiogram is by changing the position of the heart within the thorax. They have also suggested that the complete reversal of the electrical fields of the two ventricles in the thorax may result from extreme rotation of the heart about its long axis produced by an extremely large right ventricle.

Two examples of right ventricular hypertrophy are illustrated in Fig. 56. The upper set of records are those of a woman aged 34 who had pulmonary hypertension of undetermined origin, possibly a primary pulmonary vascular disorder. She had a chronic cough for four years and had developed dyspnea on exertion. Examination disclosed a presystolic gallop rhythm, accentuation of the pulmonic second sound, moderate polycythemia and roentgenographic signs of an abnormally prominent pulmonary artery. Six months after these studies were made repeated hemoptyses occurred. The limb leads display definite right axis deviation with inverted T waves in leads II and III. The mean electrical axis is plus 150 (the QRS complex is isoelectric in lead II and the axis is perpendicular to line of that lead) and the axis deviation index is minus 17. The precordial curves are quite typical of right ventricular hypertrophy. Tall R waves and relatively small S deflections are present in leads V_1 and V_2, whereas unusually small R waves and abnormally large S deflections are seen in leads V_5 and V_6. By using as a basis for comparison the record of lead I which was recorded simultaneously with each lead, it can be seen that the intrinsic deflection is distinctly later in lead V_1 than it is in leads V_5 and V_6, whereas normally the reverse is the case. The inverted T waves present in leads V_1 through V_4 are

situation must be evaluated carefully to be certain that the cardiac condition is quiescent before permitting the patient to resume his work. The best general rule is to evaluate the clinical and electrocardiographic data together. Smith[1] was among the first to describe the electrocardiogram in acute coronary occlusion and over the three decades since his report a great body of related information has been accumulated regarding the diagnosis and localization of infarction. There have been certain variations in the standard leads, which were poorly understood and occasionally such leads failed to show characteristic change of infarction even though the clinical picture was perfectly typical. Recent experience with precordial leads and certain experimental observations have clarified many of these problems and added much to our understanding of this entire field of electrocardiography.

The changes in infarction are of three types: (1) alterations in the position and configuration of the RS-T junction and segment; (2) changes in the outline of the QRS complexes, especially the appearance of large Q or QS waves and (3) alterations in the form and direction of the T waves. These changes have separate origins and individual differences are seen in the sequence with which they develop and disappear.

Displacement of the RS-T Segment

If unipolar direct leads are taken from the epicardial surface of a portion of the ventricular myocardium whose blood supply has just been interrupted by ligation of the coronary artery supplying it, the first change recorded is inversion of the T waves. This change is the result of ischemia; it will disappear if the circulation is restored. If the circulation is not restored, anoxia of sufficient duration occurs to injure the muscle. This acute injury produces upward displacement of the RS-T segment in leads from the epicardium. Such injury effects may be produced by any type of trauma to the myocardium including heat, cold, chemicals and abrasions. The injury effect is transient and lasts only so long as there is injured living muscle, that is, muscle which is dying but is not completely dead, or muscle which is recovering but is not totally recovered. As the infarct grows older the zone of injury is replaced by muscle which is merely ischemic or is dead. The degree of RS-T segment displacement tends to be maximal at the onset and to regress as the infarct grows older. It usually clears completely in 10 to 14 days after the infarction occurs in humans, whereas in dogs with infarcts produced

general features present in the upper set of records of the same illustration. The potential variations of the left leg resemble those of leads V and V6, whereas those of the left arm suggest a mixture of the potential variations of the other two extremities. The heart was apparently in the semi-vertical position.

In *summary*, it may be stated that when the heart is enlarged it is usually in the horizontal or semi-horizontal position. Left ventricular hypertrophy is associated usually with left axis deviation and a large positive axis deviation index. When the heart is in the semi-vertical position, left ventricular hypertrophy produces large R waves and inverted T waves in all leads, and the more usual changes in the electrical axis and axis index fail to appear. When the heart is in the vertical position, left ventricular hypertrophy may actually produce right axis deviation. Right ventricular hypertrophy produces right axis deviation when the heart is in the horizontal or semi-horizontal position, but when a semi-vertical position is present, large S waves appear in all the standard leads and the usual indices fail. Theoretically, right ventricular hypertrophy could produce left axis deviation if the heart were vertically placed, but such records apparently are very rare. When questions arise regarding the type of ventricular hypertrophy present, the precordial electrocardiogram will provide more reliable information than the standard leads in many instances.

Myocardial Infarction

In general, it may be said that only very rarely is the electrocardiogram persistently normal in the presence of a recent myocardial infarction. Consequently, the electrocardiogram is of great value in the diagnosis of myocardial infarction. In many instances it may confirm a diagnosis which is only suspected on the basis of the clinical findings. If the electrocardiogram is normal, the clinician's thinking may be directed along the lines of other disorders simulating coronary thrombosis and thus to the correct conclusion. Strict electrocardiographic criteria must be adhered to lest serious diagnostic errors be made. An erroneous diagnosis of myocardial infarction made on the basis of minor or equivocal electrocardiographic changes may cause a patient to suffer a great and unwarranted social, economical and psychological insult. On the other hand, if the electrocardiogram displays typical alterations of infarction and the clinical picture is incompatible with the diagnosis, the

situation must be evaluated carefully to be certain that the cardiac condition is quiescent, before permitting the patient to resume his work. The best general rule is to evaluate the clinical and electrocardiographic data together. Smith[1] was among the first to describe the electrocardiogram in acute coronary occlusion and over the three decades since his report a great body of related information has been accumulated regarding the diagnosis and localization of infarction. There have been certain variations in the standard leads which were poorly understood and occasionally such leads failed to show characteristic change of infarction even though the clinical picture was perfectly typical. Recent experience with precordial leads and certain experimental observations have clarified many of these problems and added much to our understanding of this entire field of electrocardiography.

The changes in infarction are of three types: (1) alterations in the position and configuration of the RS T junction and segment, (2) changes in the outline of the QRS complexes especially the appearance of large Q or QS waves and (3) alterations in the form and direction of the T waves. These changes have separate origins and individual differences are seen in the sequence with which they develop and disappear.

Displacement of the RS T Segment

If unipolar direct leads are taken from the epicardial surface of a portion of the ventricular myocardium whose blood supply has just been interrupted by ligation of the coronary artery supplying it, the first change recorded is inversion of the T waves. This change is the result of ischemia; it will disappear if the circulation is restored. If the circulation is not restored anoxia of sufficient duration occurs to injure the muscle. This acute injury produces upward displacement of the RS T segment in leads from the epicardium. Such injury effects may be produced by any type of trauma to the myocardium including heat, cold, chemicals and abrasions. The injury effect is transient and lasts only so long as there is injured living muscle, that is, muscle which is dying but is not completely dead or muscle which is recovering but is not totally recovered. As the infarct grows older the zone of injury is replaced by muscle which is merely ischemic or is dead. The degree of RS T segment displacement tends to be maximal at the onset and to regress as the infarct grows older. It usually clears completely in 10 to 14 days after the infarction occurs in humans, whereas in dogs with infarcts produced

experimentally it lasts only 24 hours Temporary or changing displacement of the RS T segment is the type which is so characteristic of fresh myocardial infarction If the anoxemia is of short duration the injury produced may be reversible and the changes in the RS T segment will be very transient as in some instances of angina pectoris[illegible] or coronary insufficiency[illegible] In some patients with myocardial infarction the displacement of the RS T segment will be observed to disappear only to reappear This usually means that further myocardial damage or injury has occurred either by extension of the original zone of infarction or the development of a new area of involvement It may also indicate the appearance of pericarditis Persistent displacement of the RS-T segment is rare It is usually a serious sign and has been observed in several instances in which ventricular aneurysms have developed as a sequel to infarction although the aneurysm would not seem to be responsible of itself for this particular electrocardiographic change Some examples of persistent RS T segment displacement represent continued myocardial injury[illegible] Persistent displacement of the RS T segment of the type considered here must be differentiated from that which is due merely to overlapping of the QRS complexes and T waves already discussed

The factors which determine the direction of the displacement of the RS-T segment are not completely understood[illegible] Bayley[illegible] has suggested that during diastole and systole injured muscle acts as a source of an electrical field of injury and within a zone of injury there appear to be a gradient in the intensity of polarization If a coronary artery is constricted unipolar direct leads from the epicardial surface of the affected area show upward displacement of the RS-T segment Bayley[110, illegible] has expressed the opinion that the survival of an inner lamina of uninjured or less injured subendocardial muscle may account for this upward direction Furthermore involvement of this inner subendocardial zone in some special instances may account for unexpected directions of displacement or displacements against the rule[illegible] Wolferth and associates[illegible] and Boyd and Scherf[130] have demonstrated that endocardial injuries depress the RS T segment in leads from the epicardial surface of the heart Furthermore Pruitt and Valencia[131] have shown that transmural injuries of the ventricular wall produce upward displacement of the RS T segment both in leads from the endocardial and from the epicardial surfaces of the injured region

Changes in the QRS Complexes

The alterations in the configuration of the QRS complexes associated with myocardial infarction result from the death of muscle and in unipolar direct leads these changes are recorded from the central zone of the infarct It has been observed that records made with unipolar direct leads from the epicardial surface of a transmural infarct are identical with those made by thrusting the exploring electrode into the ventricular cavity[13] There is no living muscle beneath the electrode therefore no electromotive force is being developed at that point Records from the epicardial surface of the central zone of the infarct display QRS complexes which consist of deep QS deflections representing the transmission to this surface of the initial negativity of the adjacent ventricular cavity These deep Q or QS waves usually appear while the displacement of the RS T segment is pronounced but as the latter change decreases the Q waves tend to grow more broad and deep Some muscle usually escapes destruction in an area of infarction so that there are islands of living muscle or the lesion may not be transmural If these areas of living muscle are small there will be notches on the ascending or descending limb of the QS waves due to superimposed embryonic R deflections In those infarcts in which the outer layers of muscle are relatively uninvolved the deep Q deflections are followed by R waves of small size or W shaped QRS complexes may be seen This latter type of record is recorded especially when the margins of an infarct are explored

The changes in the QRS complex which are produced by infarction tend to be permanent They may last throughout the rest of the patient s life and in some instances have been observed as long as 5 years after the acute lesion occurred Occasionally these particular alterations in the electrocardiogram may be transient The QRS changes develop early after the infarction occurs that is within a few hours but usually not quite as early as the displacement of the RS T segment With the passage of time the alterations in the QRS complexes may become less distinctive and in the case of lesions involving the anterior wall of the left ventricle the number of precordial leads displaying the typical changes may grow fewer

Changes in the T Waves

Ischemia of the myocardium produces an alteration in the manner and direction of repolarization which is reflected in a change in the contour and direction of the T waves. As mentioned earlier, if unipolar direct leads are recorded from an area of the epicardial surface while the blood supply to that area is reduced, the initial change which appears is a sharp, deep inversion of the T deflections. This disturbance appears within the first few seconds, but as the muscle becomes injured by continued anoxia the displacement of the RS-T segment overshadows and obscures the T wave inversion.[1,3] Subsequently, as the RS-T segment returns to its normal position, the inversion of the T waves reappears and grows more pronounced. Clinically it reaches its maximum development in 10 to 21 days. When direct leads are made from a zone of infarction, the most striking changes in the T waves are recorded from the margins of the infarct. The direction which the T wave takes in any lead usually proves to be opposite to the direction of the original RS-T displacement in that lead; that is, if the RS-T segment was displaced upward, the T wave becomes inverted; if the RS-T segment was depressed, the T wave will become more upright and taller than it was prior to the infarction. The typical T waves associated with infarction have a rather characteristic form with a round shoulder followed by a V-shaped inversion. They have been designated variously as "coveplane," "Pardee,"[134] or "coronary" T waves.

The changes in the T waves appear in a quite characteristic sequence which is so predictable in clinical cases that it is of significant diagnostic value, and it is also of some help in estimating the time of occurrence of the myocardial infarct. As the displacement of the RS-T segment clears, the terminal portion of the T wave begins to be inverted; this occurs in 1 to 4 days. Thereafter more and more of the later portion of the T wave comes to lie below the base line until its full development is reached in 10 to 21 days. It may be said that in patients with myocardial infarction the inversion of the T wave begins at its terminal portion and progresses back toward the QRS complex, where the inversion of the T deflection which results from digitalis begins in the initial portion of the T wave and progresses away from the QRS complex. The inversion of the T waves appears to grow more striking as more and more of the cardiac muscle changes from the injured to the ischemic state. After reaching its greatest development, the inversion of the T waves tends to regress over a period of weeks or months. The T waves may become

normal again but as a rule there is some residual abnormality although usually it is not nearly so characteristic as during the first weeks after the infarct occurred

It has been indicated that although they are all a part of the electrocardiographic picture of infarction the deep QS deflections the RS T segment displacement and the inversion of the T waves arise from different zones of the involved area Since this is true unipolar direct leads from the epicardial surface of an infarct do not show all these changes present in a single lead Semi direct leads—and precordial and esophageal leads fall into this category—are recorded from points which are at some distance from the epicardial surface Such leads record the potential variations which are occurring over a much larger area of the heart s surface and frequently show a combination of all three types of changes Occasionally such leads do show QS deflections from some points over the thorax and more striking T wave inversion in leads from adjacent points as if the former arose from the center and the latter from the margins of the infarct It is well to remember that the change in the RS-T segment predominates during the earliest stage of infarction because the area which is anoxic enough to be injured is larger than that whose blood supply is reduced only to the point of ischemia As the infarct heals this ratio becomes reversed and finally the changes in the T waves predominate There may be a stage in the healing process when the areas of injury and ischemia are of relatively equal size At this stage the changes in the RS T segment and T waves may cancel each other If electrocardiographic observations are made for the first time at this stage the characteristic changes may fail to appear The studies must be repeated at a later date when further healing has occurred in order to make the correct diagnosis

The diagnosis of myocardial infarction can be made from the electrocardiogram alone only if there are typical changes in both the QRS complexes *and* the RS T segment or the T waves Adherence to this rule will prevent serious diagnostic errors The changes may be confined to the QRS complexes in cases of old myocardial infarction and although such abnormalities are of more significance than changes in the T waves usually there must be corroborative clinical data to permit a definite diagnosis There are several conditions which produce inversion of the T waves resembling that occurring in infarction The diagnosis of coronary thrombosis based upon alterations in the T waves alone is therefore hazardous unless it is supported by clinical data and serial curves showing the characteristic progression and regression of the

changes Sequential changes of this type occur in few other conditions except pericarditis which usually can be excluded on the basis of clinical findings

Localization of Myocardial Infarction

The potential variations of the epicardial surface of the infarcted region are transmitted to the adjacent parts of the body Consequently, although the changes in form of the electrocardiogram resulting from the lesion are fundamentally the same in all cases the size and location of the infarct and the position of the heart within the chest determine the leads in which these changes appear If the anterior wall of the left ventricle is involved the changes are most striking in leads from the central precordial area if the anterolateral wall of the same chamber is infarcted leads from the anterolateral aspects of the left hemithorax and the left arm display the typical abnormalities, if the lesion is located in the posterior or diaphragmatic area of the left ventricle the alterations appear in records taken from the esophagus back and left leg The changes appear in the limb leads when the infarct is so located that its potential variations are transmitted toward the left shoulder or the pelvis Records taken from points on the surface of the body on the same side as the region of the heart involved show changes resembling those which would be recorded from the epicardial surface of the lesion Those parts of the body on the side of the heart opposite that involved show changes which are the inverse of those occurring at the surface of the lesion, that is, the RS T segment is depressed during the very acute stages, and the T waves later become upright at such points

The electrocardiographic patterns which are diagnostic of myocardial infarction have been classified according to the leads in which the typical changes in the QRS and T complexes appear[7, 8] These patterns have been designated according to the region of the left ventricle which is involved Such a classification permits accurate localization of the infarction and adds to our understanding of the electrocardiographic problems involved but its major purpose is to emphasize the fact that in order to obtain unequivocal electrocardiographic evidence of infarction extensive electrocardiographic exploration may be required In some cases the most typical changes may be recorded in special leads from the back the esophagus the ensiform process the higher regions of the left anterior chest or still other regions than those studied routinely

Anteroseptal Infarction — The characteristic changes in both the QRS complexes and the RS-T segment and T waves are confined to one or more of the first four standard precordial leads (V_1, V_2, V_3 or V_4). Leads V_5, V_6, V_L and I may show more or less typical changes in the T waves but no distinctive changes in the QRS complexes occur in these records. Prominent Q waves sometimes appear in leads II and III. Leads I and V_L display potential variations such as occur over the anterolateral aspects of the left ventricle and consequently show no greater changes in the QRS complexes than do leads V_5 and V_6. The standard leads may be so nearly normal in patients with lesions of this type that the diagnosis may be missed unless records from the right side of the precordium are taken. Postmortem studies have shown that infarcts of this type involve the anteroseptal wall of the left ventricle. Examples of lesions of this type are shown in Figs 66 and 68. In the first of these the standard leads show only very slight inversion of the T waves in lead I and lead V_F displays somewhat deeper inversion of the T deflection. Diagnostic changes in both the QRS complexes and T waves are confined to lead V_2 although deep inversion of the T deflection occurs in leads V_3, V_4 and V_5. In the second example (Fig 68) the characteristic changes in the QRS complexes and T deflections are confined to leads V_2 and V_3 with inverted T waves in leads V_4 and V_5 and almost no change at all in the standard leads. Lead V_F in both cases is entirely normal.

Anterolateral Infarction — The diagnostic changes in the QRS complexes and T waves are in lead V_5 in leads V_4, V_5 and V_6 or in some such combination of the standard precordial leads which does not include leads from the right side of the precordium. There are similar changes in lead I and V_L because the infarct is so located that the potential variations at its epicardial surface are transmitted to the left arm.

The records illustrated in Fig 57 are those of a man aged 55 who had a severe attack of pain in the left hemithorax and upper abdomen on March 13 1941. He recovered satisfactorily but on May 15 1941 there was a sudden onset of complete aphasia probably due to a cerebral embolus. Examination of the heart was negative except for moderate cardiac enlargement. The electrocardiograms illustrated taken on May 16 1941 show diagnostic evidence of infarction in leads I, V_L, V_3, V_4, V_5 and V_6. The R wave increases in height in normal subjects as the exploring electrode is moved across the precordium from the first to the fourth position and then it decreases somewhat as the electrode is moved farther to the left[8]. In this case the R wave can be seen to decrease in height as the exploring electrode was moved to the left disappearing

in leads V[illegible] and V[illegible] this is a more reliable sign of infarction than absence of the R wave in the first two or first three precordial leads

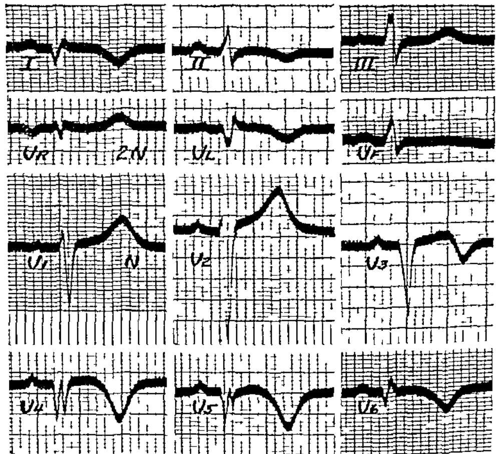


Fig 57 Anterolateral myocardial infarction The characteristic deep Q or QS deflections and terminal inversion of the T waves are seen in leads I, V[illegible], V[illegible], V[illegible], V[illegible] and V[illegible] Note the progressive decrease in the height of R from lead V[illegible] to lead V[illegible] This patient aged 55 had an attack of severe pain in the chest and abdomen two months earlier and sudden complete aphasia on the day before these records were made

Extensive Anterior Infarction — These cases may be considered a combination of anteroseptal and anterolateral myocardial infarction Leads I and V_L and all of the six standard precordial leads or all except lead V_1 show the characteristic signs of infarction Records of this type are associated with very large infarcts and in one example familiar to the author the lesion measured 9 by 10 cm If the patient recovers the

number of precordial leads displaying the typical changes often decreases as the lesion heals and becomes fibrotic

High Anterolateral Infarction — There are diagnostic changes in leads I and V_L and in unipolar leads from parts of the left side of the precordium or of the anterior aspects of the left side of the chest that are nearer the left shoulder than those from which leads V_4, V_5 and V_6 are taken. The complexes of some of the standard precordial leads from the left precordial area are abnormal but show much less pronounced changes than those exhibited by the leads mentioned.[ ]

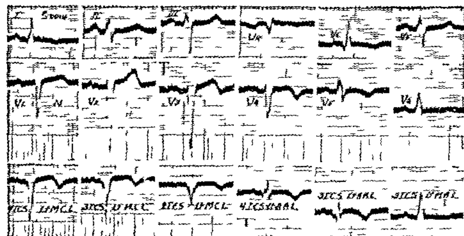


Fig 58 High anterolateral myocardial infarction. Leads I and [illegible] display small Q waves and terminal inversion of the T waves. The R deflections are unusually small in leads [illegible] and [illegible], and there is terminal inversion of T in leads [illegible], [illegible] and [illegible]. But large Q or QS deflections are not seen in any of the usual precordial leads. Large QS deflections and inverted T waves were recorded from points in the left midclavicular line at the level of the fourth, third and second intercostal space. Patient was a man aged 41 who had severe angina pectoris followed by hemiplegia one year earlier (From an article by Rosenbaum and associates[ ])

The electrocardiograms shown in Fig 58 are those of a man aged 41 who had severe angina pectoris for a brief period one year earlier. Two weeks after the pain began he suddenly developed a left hemiplegia. The clinical examination at the time of observation disclosed a persistent left hemiplegia and slight cardiac enlargement. The standard and unipolar limb leads show slight left axis deviation with small Q waves and slight terminal inversion of the T deflections in leads I and V_L. The

usual precordial leads show tiny Q waves in leads V V_3 and V_4 and distinct terminal inversion of the T waves in leads V_3 V_4 and V In these leads the R wave failed to grow progressively taller as the electrode was moved from the first to the fourth position Additional records from points in the left mid clavicular line but one and two intercostal spaces higher than the usual level display both large QS deflections and sharp terminal inversion of the T waves changes which are characteristic of myocardial infarction As in most cases of this type the routine studies are abnormal and there were clinical findings which were compatible with the diagnosis of myocardial infarction but special electrocardiographic exploration was required to record the most typical findings

Plain Posterior Infarction — Diagnostic changes are present in lead V_F and in both leads II and III or in one or the other There are similar changes in leads from the ventricular levels of the esophagus i e points which are at least 10 cm below that level at which the largest auricular deflections are recorded The standard precordial leads usually show downward RS-T displacement in the earliest stages of infarction and in the later stages often show abnormally large R and T waves in the leads from the right side of the precordium

The man whose electrocardiograms are shown in Fig 59 was aged 45 years He had symptoms typical of acute coronary thrombosis one month before these curves were taken The prominent Q waves and sharply inverted T waves present in both leads II and III are characteristic of a recent posterior infarction The typical changes of infarction are seen in lead V_F and from the ventricular levels of the esophagus (leads L and L_{44}) since the infarct involved the posterior and diaphragmatic aspects of the left ventricle and the potential variations of the epicardial surface of the lesion were transmitted toward the esophagus and left leg Lead L_3 represents the auricular level in the esophagus because the P waves are large and display an intrinsic deflection The QRS complexes at this level commonly display large Q or QS waves since the exploring electrode is opposite the great valvular orifices and the initial negativity of the ventricular cavities is transmitted to it As is usually the case in posterior lesions the precordial leads in this patient show larger R waves and taller more upright T waves in leads V_1 V and V_3 than is normal No changes are present in the RS-T segments since the acute injury stage has passed but in lesions of this type during the earliest stages there is upward displacement in leads II III and V_F and in records from the ventricular level of the esophagus and downward displacement in lead I and in records over the right precordium

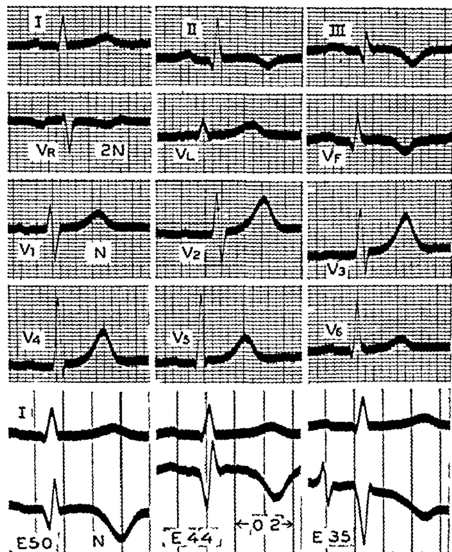


Fig. 59. Posterior myocardial infarction. Large Q waves and typically inverted T waves are found in leads II, III, V_F and near this from the ventricular levels in the esophagus lead E_{50} and E_{44}. (Symbol E signifies unipolar esophageal leads and subscript indicates distance in centimeters of electrode from the nares.) Note the large P waves which exhibit an intrinsic deflection in lead E_{35} from the auricular level. The precordial leads are normal except for rather tall R and T waves in leads V , V and V_4. This man, aged 45, had symptoms of an acute myocardial infarction one month earlier. (From an article by Wilson and associates.)

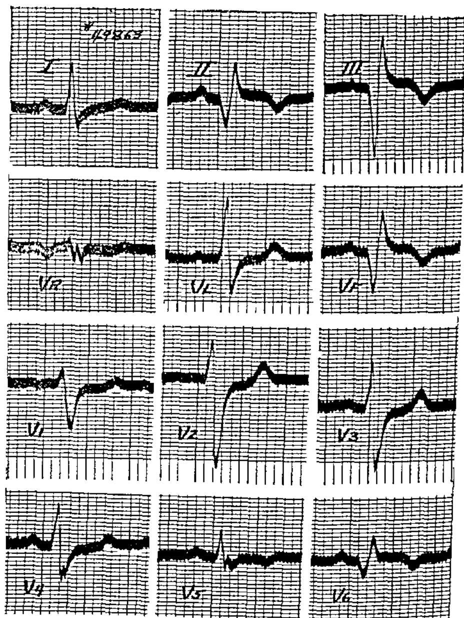


Fig 60 Posterolateral myocardial infarction The typical changes in both the QRS complexes and T waves are found in leads II III V_F and V Inverted T waves are present also in lead V Infarcts in this location differ from plain posterior lesions because the alterations appear in leads V and V This man aged 61 had an attack of severe pain in the chest seven months earlier and a second attack began a few days before these electrocardiograms were made (From an article by Wilson and associates[26])

Posterolateral Infarction — Electrocardiograms of this type differ from those of posterior infarction only in that the typical changes in the QRS complexes and T waves are present also in lead V_5 or leads V_5 and V_6. The T waves are inverted frequently in leads I and V_5. These features are present because the infarct is either located in or extends around to the posterolateral aspects of the left ventricular wall.

The records reproduced in Fig 60 are those of a man aged 61 years who was seen on June 18, 1944. He had an acute myocardial infarction in November 1943. A few days before he was admitted he had a second attack of precordial pain following moderate exertion. Tarry stools were noted soon thereafter. In the early morning of the day that these electro

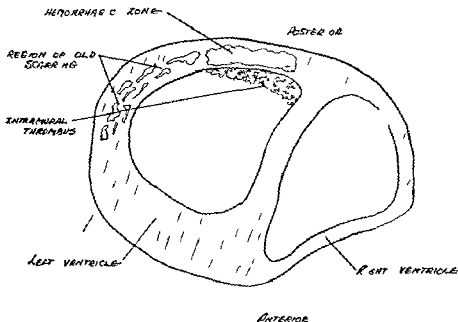


Fig 61. Diagram of a transverse section of the heart at postmortem examination of the patient whose electrocardiograms are illustrated in Fig 60. An old posterolateral infarct and the more recent posterior lesions are shown. The patient also had a perforating gastric ulcer complicated by a subphrenic abscess and fibrinopurulent peritonitis. (From an article by Wilson and associates.)

cardiograms were made he developed severe pain in the left chest and abdomen. He was in shock, the heart sounds were faint, and the abdomen was rigid when he was admitted to the hospital. He died on the following

day. The sketch shown in Fig. 61 illustrates the old posterolateral and fresh posterior infarcts which were disclosed by the postmortem examination. There was also a perforating gastric ulcer with fibrinopurulent peritonitis and a subphrenic abscess. The typical signs of infarction in this patient are seen in leads II, III, V_1 and V_F. The T waves are also abnormal in lead V. The abnormalities in leads V and V_F as well as the characteristic changes in leads II and III lead to the antemortem diagnosis of posterolateral infarction.

Posteroinferior or Posteroseptal Infarction.—Cases of this type resemble posterior myocardial infarction so far as the standard and unipolar limb leads are concerned, but in addition there are abnormally large Q or QS deflections and upward RS-T displacement or sharply inverted T waves in lead V_1 (ensiform) and sometimes in lead V_1. Records of this type are uncommon.

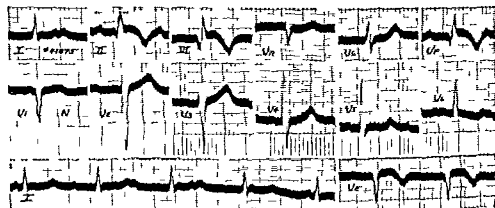


Fig. 62. Posteroinferior or posteroseptal myocardial infarction. Prominent Q waves and deeply inverted T waves are present in leads II, III and V. In addition to these features typical of posterior lesions, large QS deflections and inverted T waves are seen in lead V_F. This change suggests that the infarct extended up onto the inferior apical aspects of the heart. Complete atrioventricular heart block, which was also present, is seen in the lower, longer strip of lead I. Records from a male aged 53, who had precordial mild discomfort one week earlier. (From an article by Wilson and associates.)

The patient, whose records are shown in Fig. 62, was a man aged 53 years, who had numbness in the arms on December 19, 1941 and a brief, sharp retrosternal pain four days later. Thereafter his chest felt "bruised" for several days. These electrocardiograms, recorded on December 26, 1941, show upward displacement of the RS-T segment, sharply inverted T waves and prominent Q waves in leads II, III and V_F. Complete heart block, which proved to be transient, was present also

This arrhythmia occurs rather commonly as a complication of posterior myocardial infarction especially if the lesion involves the septum[6]. The striking feature in this patient is that there are also typical signs of infarction in the unipolar lead from the tip of the ensiform process (lead V_E). There is no R wave in lead V_1 and the R deflection in lead $V_{[illegible]}$ is small in contrast to the large R waves usually seen in these leads in cases of posterior infarction. The infarct in this case probably extended up onto the inferior apical aspects of the heart or the peculiarity may have resulted from an unusual position of the heart.

High Posterolateral Infarction — The electrocardiogram in cases of high posterolateral infarction resembles those in patients with high anterolateral infarction except that the prominent Q waves and inverted T waves appear in leads from the upper left axilla and the upper left back rather than upper parts of the anterior left chest[1]. The records from the right side of the precordium resemble those seen in posterior infarction.

Variations From the Usual Pattern in Myocardial Infarction

It has been shown that the location of the infarction in the heart and to some extent the position of the heart within the thorax determine the particular leads which show the changes which are sought for in the electrocardiogram to substantiate the clinical diagnosis. There are variations other than those of localization. The changes may be confined to the T waves alone, the alterations in the QRS complexes may be unusually transient, all the abnormalities may be unusually persistent, or other deviations from the expected pattern or sequence may be observed. All of the factors responsible for these variations are not clearly understood but it is well for the physician to be familiar with them in order that they be recognized and properly evaluated.

T Wave Changes Only

The patient whose electrocardiograms are shown in Fig. 63 was a physician aged 67 years who was seen first on August 7, 1934. The standard limb leads showed moderate left axis deviation but no other abnormalities. In March 1940 he had an attack of severe pain in the chest accompanied by a fall in blood pressure. Electrocardiograms were taken first on April 5, 1940, six weeks after the attack occurred. The

standard limb leads show only minor differences from those taken six years earlier The precordial curves show sharp terminal inversion of the T waves in all leads but no significant changes in the QRS complexes Five months later the inversion of the T waves was much less striking and eight months later all electrocardiographic evidence of infarction had disappeared This patient made a complete recovery and returned to active practice He died in 1945 from a neoplasm of the biliary tract

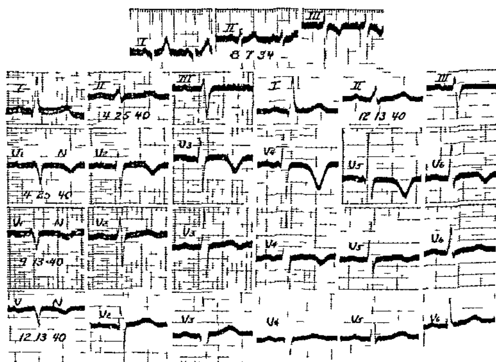


Fig 6 Anterior myocardial infarction with transient T wave changes only August 7 1934 Standard leads show slight left axis deviation April 5 1940 Deep terminal inversion of the T waves is present in all of the precordial leads but there are no significant changes in the QRS complexes September 13 1940 The T waves are still slightly inverted in leads V and V December 13 1940 The standard and precordial leads are normal except for slight left axis deviation This man aged 67 years had pain in the chest and a fall in blood pressure in March 1940 He recovered completely and died five years later of a disorder unrelated to the heart (From an article by Wilson and associates[9])

The diagnosis of myocardial infarction can be made on the basis of T wave or RS-T segment changes alone only if a characteristic sequence of alterations such as that shown here is observed Even if such a sequence is recorded it is usually best to be certain that the clinical

picture is compatible with the diagnosis. The diagnosis is almost never justified from a single record which shows changes confined to the T waves and RS-T segments. It is probable that infarcts that give rise to changes of this type are relatively small in their extent or they may be in an unusual location in respect to the type of leading now employed. Most patients with infarcts of this type do well and have no serious impairment of function upon recovery.

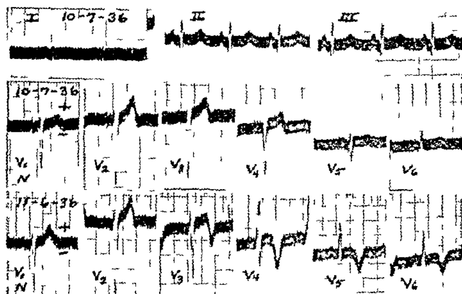


Fig. 64. Anterior myocardial infarction with transient QRS changes. October [illegible] 1936 the standard leads show extremely small QRS complexes and flat T waves in all leads. In the precordial leads the R waves decrease in size from lead V[illegible] to V[illegible] and deep QS waves occur in lead V[illegible]. R is also abnormally small in leads V[illegible] and V[illegible]. November 6, 1936 the QRS complexes in the precordial leads have become normal but deeply inverted T waves are seen in leads V[illegible], V[illegible], V[illegible] and V[illegible]. This man aged 54 years had burning retrosternal discomfort and dyspnea on October 6, 1936, eight days following a transurethral resection for prostatic hypertrophy. His recovery was complete and uneventful. (From an article by [illegible] and [illegible].)

Transient QRS Changes

The records reproduced in Fig. 64 are those of a man aged 54 years who had a transurethral resection for benign prostatic hypertrophy on September 9, 1936. On October 6 he began to have a burning sensation

beneath the sternum and dyspnea Examination disclosed an ashen pallor, a gallop rhythm a fall in blood pressure leucocytosis and fever The standard electrocardiogram taken on the following day shows abnormally small QRS complexes and flat T waves in lead I The precordial leads show a progressive diminution of the size of the R deflection (the reverse of normal) with deep QS deflections in lead V_4 One month later there was sharp terminal inversion of the T waves in all of the limb leads and the last four precordial leads but the QRS complexes were normal The patient's recovery was complete and uninterrupted Instances such as this are uncommon because the QRS changes tend to be persistent whereas alterations in the T waves usually are more transient In this case the reverse was true It is possible that in the early stages in such cases the infarcted muscle is incapable of responding to the excitatory impulse but it is not dead and subsequently recovers its excitability

Persistent QRS and T Wave Changes

The characteristic evolution and regression of changes associated with infarction has been described Changes in the QRS complex commonly undergo an incomplete retrogression and the disappearance of the T wave abnormalities usually is very striking Occasionally however, all of the typical changes will persist for many years I have seen one instance in which there were still diagnostic abnormalities twenty five years after the myocardial infarction occurred An example of this type of persistent change is illustrated in Fig 65 This patient had symptoms of an acute coronary thrombosis in May 1934 when he was 43 years old Electrocardiograms taken in July 1934 were not significantly different from those reproduced When examined on May 17 1941 he was working regularly and had no symptoms other than slight dyspnea on exertion he had no further attacks of chest pain after the initial infarction The records show diagnostic changes of infarction in leads V_3 and V_4 This is an anteroseptal or anterior lesion in its location This is also an instance in which lead V_1 shows more significant changes than lead I

Persistent displacement of the RS T segment is also seen occasionally This is more difficult to account for than persistent abnormalities of the type just described It has been seen in association with ventricular aneurysm[116] but in other cases no aneurysm has been demonstrable Recently

I have observed a case with a massive ventricular aneurysm disclosed by the postmortem examination but there was no persistent elevation of the RS T segment It is possible therefore that the association of this electrocardiographic change with ventricular aneurysm is due to chance rather than to any etiological relationship

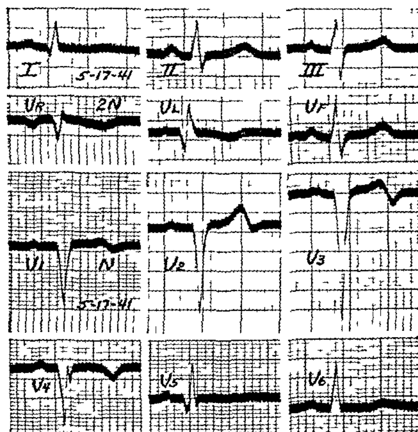


Fig 73 Anterior myocardial infarction with persistent QRS and T wave abnormalities Large QS deflections are present in leads V V V and V and inverted T waves are seen in leads V V and V. Note that lead I and V resemble lead V This man had a myocardial infarction in May 1934 at age 23 years These records made seven years later are not significantly different from others made in July 1934 The patient was working regularly and had been free of chest pain (From an article by Wilson and associates)

Anteroseptal Infarction With Lateral Extension

In the discussion of anteroseptal myocardial infarction it was pointed out that the standard and unipolar limb leads usually show only minor abnormalities whereas the leads from the right precordium disclose diagnostic changes In some cases of this variety the initial infarct suddenly grows larger either by extending laterally or because a new zone adjacent and lateral to the original one becomes infarcted The diagnosis of such a sequence of changes can be made from the electrocardiograms if they are taken at the appropriate intervals[17]

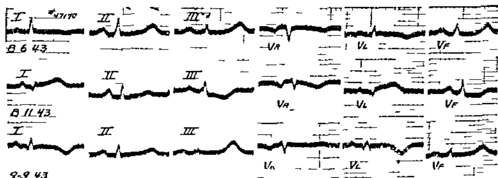


FIG 66 Anteroseptal myocardial infarction with lateral extension August 6 1943 standard and unipolar limb leads taken six and one half hours after the onset of symptoms show only rather small QRS complexes and slightly inverted T waves in leads I and V_L August 11 1943 four days after the second attack of pain There is now distinct elevation of the RST segment in leads I and V_L, depression of the RS T segment in leads III and V_F and small bizarre QRS complexes with prominent Q waves in leads I and V September 9 1943 the displacement of the RS T segment has cleared and inverted T waves are now present in leads I and V_L Patient was a 43 year-old housewife whose symptoms began on August 6 1943 and who had an extension of the original lesion on August 194 (From an article by Rosenbaum and associates[17])

The records reproduced in Figs 66 and 67 are from a 43 year old housewife, who had moderately severe oppressive precordial pain on August 6 1943 The standard leads taken six and one-half hours later (upper row Fig 66) show only slightly inverted T waves in lead I and sharper terminal inversion of the T waves in lead V_L There are no significant changes in the QRS complexes The precordial leads recorded twenty seven hours after the onset of symptoms (upper row, Fig 67) show diagnostic evidence of infarction in lead V and inverted T waves in leads V_1, V V_3 V_4 and V The infarct was therefore anteroseptal in its location Thirty six hours after the initial attack the precordial

distress recurred and persisted for thirty six hours despite large doses of opiates Electrocardiograms taken on August 9 and August 11 (middle rows Figs 66 and 67) show prominent Q waves small or absent R waves and upward displacement of the RS T segment in leads I V_L V V_3 and V_4 Lead III shows downward displacement of the RS T segment Since the diagnostic changes originally were confined to lead V and now are also present in leads V_3 and V_4 it is evident that the original zone of infarction had extended laterally The displacement of the RS T segment is further evidence of fresh myocardial injury When in the course of following a patient with recent myocardial infarction by means of serial electrocardiograms there is such a recrudescence of upward

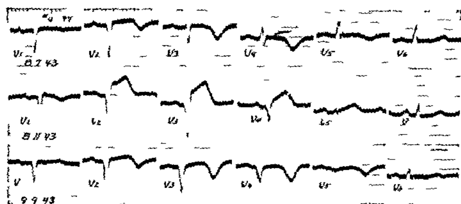


FIG (Anteroseptal myocardial infarction with lateral extension August 7 1943 precordial leads taken twenty-seven hours after the onset of symptoms show QS deflections confined to leads V and inverted T waves in leads V V_2 V_3 V and V_6 August 11 1943 large QS waves now are present in leads V V and V indicating that the infarct has extended laterally The appearance of striking elevation of the RS T segment also suggests that new areas of muscle have become involved September 9 1943 the usual progressive changes have occurred with deep inversion of the T waves in those leads which previously displayed upward displacement of the RS-T segment Same patient as Fig 66 (From an article by Rosenbaum and associates[137])

displacement of the RS T segment it is well to study the patient carefully for the possibility of new zones of infarction The final records in this patient (lower rows Figs 66 and 67) display the expected progression of changes The displacement of the RS T segment has disappeared and the T waves now are sharply inverted in those leads in which there was originally upward displacement of the RS T segment

Several observers have pointed out that myocardial infarction may

be preceded by premonitory or prodromal pain[134, 139, 140] The initial discomfort experienced by the patient described here might have been ascribed to prodromal pain of an impending myocardial infarction if the original precordial electrocardiograms had not been recorded The second more severe attack would then have been considered the initial infarction The true situation was disclosed by the electrocardiographic studies It is apparent that at least some attacks of so called prodromal pain represent actual myocardial infarction[137, 141]

Anteroseptal Followed by Posterolateral Infarction

Electrocardiographic observations may localize a second infarction occurring in a patient who has had an earlier lesion in quite another part of the heart It is of interest to study the influence of the second infarct upon the electrocardiographic changes produced by the first since the original alterations may be greatly obscured or made to practically disappear

The electrocardiograms illustrated in Figs 68 and 69 are those of a man aged 48 years who had an acute coronary thrombosis on May 21, 1938 The series of records shown in Fig 68 indicate that the initial infarct was of the anteroseptal type The first observations were made two hours after the onset of symptoms The standard leads show no significant changes but there is pronounced upward displacement of the RS-T segment in leads V V_3 and V_4 Records made three days later show large QS waves in leads V_1 V and V_3 and the RS T segments and T waves display the typical progressive changes Over a period of nine months the T deflections returned to their normal form but the changes in the QRS complexes persisted

Late in February 194 the patient again began to have severe cardiac pain Electrocardiograms taken on March 5 194- show only the residual changes of his initial anteroseptal infarction (Fig 69) He continued to have frequent attacks of angina pectoris and on March 11 he had a severe prolonged attack Once again records were taken within two hours after the onset of symptoms The limb leads show prominent Q waves and elevation of the RS T segment in leads II and III The precordial leads show slight elevation of the RS-T segments in leads V_5 and V_6 Because the typical changes produced by the second infarction were in leads II III V and V_6 it was classified as a posterolateral lesion It is interesting to observe that the second infarct nullified the

changes of the initial lesion and actually made the records from the right precordium more normal

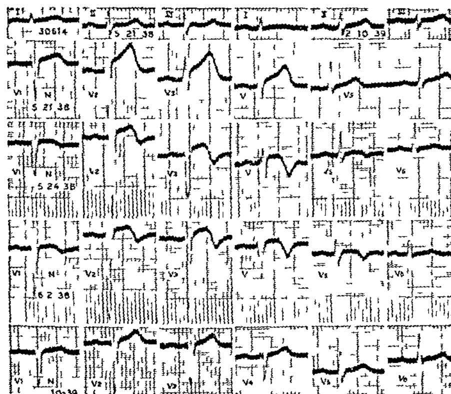


Fig 68 Anteroseptal myocardial infarction May [illegible] 1938 record taken two hours after the onset of symptoms shows elevation of the RS-T segments in leads V1, V2 and V3. May 24 1938 large QS waves are now present in leads V1, V2 and V3 with beginning inversion of the T waves and decreasing elevation of the RS-T segments in leads V1, V2 and V3. June [illegible] 1938 there is continued progressive change in the T waves. February 9 1939 the changes in the QRS complexes in leads V1, V2 and V3 persist but the T waves have become upright. Note that the standard leads are normal and fail to give any indication of the abnormalities present over the right precordial area. This man aged 48 years made a satisfactory recovery. For the subsequent posterolateral infarction see Fig 69 *(From an article by Wilson and associates.)*

The electrocardiographic diagnosis and localization of myocardial infarction is distinctly more difficult when there are two or more lesions present simultaneously which differ in age size and location. When posterolateral infarction follows an anteroseptal lesion Q deflections and

inverted T waves make their initial appearance in lead V_6, any residual inversion of the T waves over the right precordium is abolished, and embryonic R waves in leads V and V_3 rise above the isoelectric level The picture is often bizarre and atypical when more than two infarcts coexist

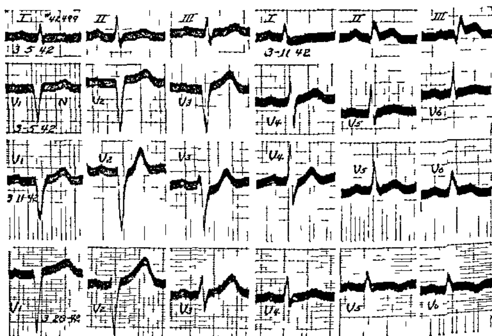


Fig 69 Posterolateral myocardial infarction following an anteroseptal infarction March 5 194 standard and precordial leads are similar to those taken on February 9 1939 (Fig 68) March 11 194 standard and precordial leads taken two hours after onset of severe precordial pain there are small Q waves and elevated RS T segments in leads II III and V March 28 194 the T waves have become inverted in leads V and V Note that R waves reappeared and the T waves grew taller in leads V V and V after the posterolateral infarction For earlier anteroseptal infarct see Fig 68 (From an article by Wilson and associates[9])

Myocardial Infarction Complicated by Bundle Branch Block or Arborization Block

Myocardial infarction almost always occurs in the wall of the left ventricle or in the interventricular septum It has been pointed out that in infarction the characteristic changes in the QRS complex are due to the transmission of the initial negativity of the left ventricular cavity to

the epicardial surface of the lesion When right bundle branch block is present, this initial negativity of the left ventricular cavity is unaltered when an infarct is also present this negativity is transmitted to the epicardial surface of the infarct or to the right ventricular cavity if the lesion involves the septum[11] On the other hand left branch block causes the left ventricular cavity to be initially positive when an infarct is present this initial positivity is transmitted to the epicardial surface of the involved area and typical large Q or QS deflections do *not* occur[11] The only exception to this rule is the relatively uncommon circumstance in which there is also transeptal infarction for in such a case the initial negativity of the right cavity is transmitted to the left

When anterior infarction is complicated by right bundle branch block the standard leads usually fail to display typical changes There are usually prominent Q waves and tall late R deflections in leads from the right precordium The latter are due to delayed activation of the free wall of the right ventricle Large Q waves or QS waves are recorded from points farther to the left which overlie the infarct more directly[1] Characteristic changes in the RS T segment and T complex are present also usually if the infarct is a recent one When posterior infarction is complicated by right bundle branch block abnormalities of the QRS and T complexes which are quite characteristic of infarction are present in leads II III and V_F[113] The records taken from the right side of the precordium are quite similar to those in uncomplicated right branch block

Left bundle branch block complicated by infarction of the free wall of the left ventricle is seldom associated with characteristic changes in either the limb leads or in records from the precordium[11] As indicated previously the reason for this is that when left branch block is present the cavity of the left ventricle is initially positive when the QRS complex is being inscribed The large Q or QS deflections which are the typical sign of infarction sought for cannot occur at the surface of the infarct and in leads from adjacent parts of the body surface Changes in the T waves which are suggestive of infarction do occur occasionally especially if the sum of the areas of the positive and negative deflections of the QRS complex is small If this net area is large its effect is to obscure any typical changes in the T deflections Changes in the QRS complex characteristic of infarction are seldom seen in left branch block complicated by posterior infarction[113] The initial positivity of the left ventricle in left bundle branch block is produced by activation of the right half of the interventricular septum Consequently if an infarct of the

left ventricle also involves the septum extensively enough the electrocardiographic diagnosis of infarction may be made possible through the appearance of large Q or QS deflections representing the negativity of the right ventricular cavity in leads from the precordium, even though left branch block is present[144]

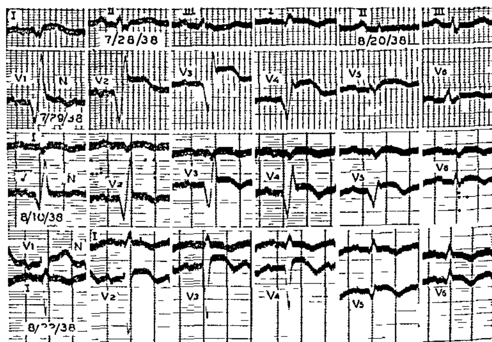


Fig. 10 Anterior myocardial infarction complicated by transient right bundle branch block July 8 1938 the standard leads show only small bizarre QRS complexes in all leads July 9 1938 the precordial leads show large Q waves and distinct elevation of the RS T segment in leads V V and V changes typical of a fresh anterior infarction The QRS interval is abnormally long and large and late R deflections are present in leads V and V indicating right branch block August 10 1938 right branch block still present but inversion of the T waves has appeared August 2 1938 the bundle branch block has cleared and the changes in the QRS complexes are now seen in leads V V and V The QRS interval is normal and the large R deflections are no longer present in leads V and V This man aged 37 years had severe anginal pain on July 6 and 8 1938 Postmortem examination on September 18 1938 disclosed a large anterior myocardial infarction with central liquefaction (From an article by Wilson and associates[9])

Anterior Infarction Plus Right Bundle Branch Block

The records illustrated in Fig 70 are those of a man aged 37 years who had severe anginal pain on July 6 and 28 1938 A pericardial friction sound was heard two days later He died on September 18 1938 and autopsy disclosed a very large anterior infarction with liquifaction necrosis of its central portion and adhesive pericarditis over its surface The standard leads taken on July 8 show only small bizarre QRS complexes with a QRS interval measuring 0 12 sec and slight upward displacement of the RS T segment in lead I The precordial leads taken on the following day show large late R deflections in leads V_1 V and V_3 but no early small initial R waves such as occur in these leads in uncomplicated right branch block The presence of anterior infarction is indicated by the large Q deflections in leads V_1 V V_3 and V_4 the small bizarre QRS complexes in lead V and the pronounced upward displacement of the RS T segment in leads V V_3 and V_4 The precordial leads taken 11 days later show less RS T displacement and terminal inversion of the T waves in all leads The records taken on August 2 indicate that the intraventricular block had cleared The QRS *interval is of normal duration and there are diagnostic changes of infarction* in leads I V_4 V and V_6 Small initial R waves are now present over the right precordium and the large late R deflections previously recorded from this zone are seen no longer The progressive decrease in the size of the R deflection from lead V_1 to lead V_4 is especially noteworthy as a sign of infarction This infarct may be classified as an anterolateral lesion

Posterior Infarction Complicated by Right Bundle Branch Block

The electrocardiograms reproduced in Fig 71 are those of a man aged 49 years who had aching retrosternal pain accompanied by faintness seven days earlier Physical examination disclosed slight cardiac enlargement the blood pressure was 105/80 mm Hg The standard leads taken on April 4 1938 are strongly suggestive of a recent posterior myocardial infarction The patient returned on April 19 1943 because *of intermittent claudication angina pectoris on effort and symptoms of* peptic ulcer The limb leads on the second occasion again show prominent Q waves in leads II III and V_F suggestive of posterior infarction but the T waves are not as characteristic as they were five years before

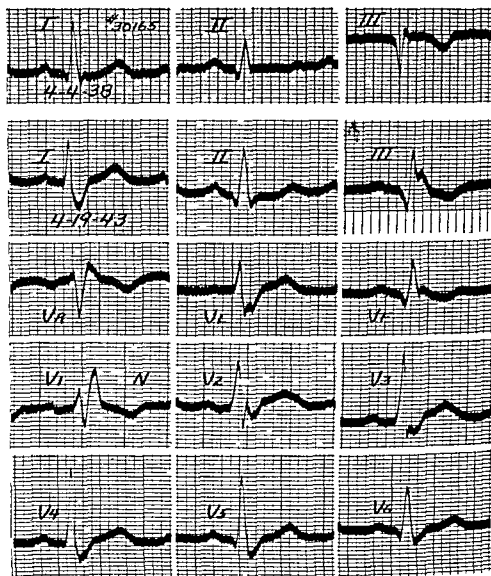


FIG 71 Posterior myocardial infarction complicated by right bundle branch block April 4 1938 the standard leads show small Q waves and slightly inverted T waves in lead II large Q waves and deeply inverted T waves in lead III These changes suggest a posterior infarction Patient had retrosternal pain and faintness seven days earlier April 19 1943 standard and unipolar limb leads show widened QRS complexes with broad slurred S waves in leads I and V_L Prominent Q waves persist in leads II III and V_F Precordial lead V shows the typical changes of right branch block In this case the right branch block did not obscure the evidence of posterior infarction (From an article by Wilson and associates[133])

The QRS interval is 0 1 sec and broad slurred S waves are present in lead I These changes suggest right bundle branch block a diagnosis confirmed by the precordial electrocardiograms The large late R deflection in lead V_1 and the broad slurred S waves recorded over the left precordium are typical of right branch block It is evident that in this case the development of delayed activation of the right ventricle did

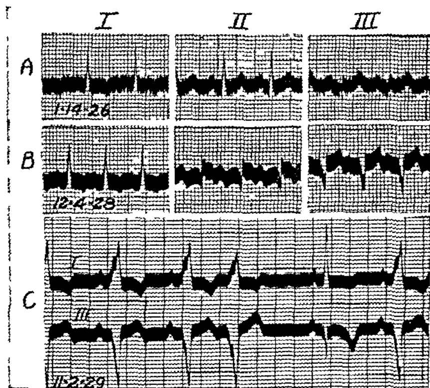


Fig 72 Posterior myocardial infarction complicated by left bundle branch block January 14 1926 standard leads are abnormal because of slightly inverted T waves in lead I the patient was complaining of precordial pain and dyspnea December 4 1928 large Q waves and elevated RS T segments are present in leads II and III These changes are typical of a fresh posterior infarction The patient had typical symptoms two days earlier November 2 1929 leads I and III recorded simultaneously show changes typical of left bundle branch block The fourth beat recorded is an auricular extrasystole it is followed by a pause of considerable length and block is not present in the next normal cycle When block is not present large Q waves and deeply inverted T waves are seen in lead III The latter change is entirely obscured when the block is present (From an article by F N [illegible])

not obscure the changes in the QRS complexes due to the earlier posterior infarction

Posterior Infarction Complicated by Left Bundle Branch Block

The records shown in Fig 72 are those of a man aged 63 years who was having angina pectoris when the first examination was made on January 14 1936 The standard leads at that time showed only slight inversion of the T waves in lead I On December 2, 1938 he had symptoms characteristic of acute coronary thrombosis The electrocardiogram taken two days later shows prominent Q waves and distinct upward displacement of the RS-T segment in leads II and III, changes typical of a fresh posterior myocardial infarction Records made eleven months later show left bundle branch block When the intraventricular block is present the electrocardiographic signs of the posterior infarction are obscured At one point however, an auricular premature beat occurred The first impulse after the post-extrasystolic pause spread normally over the ventricles When this occurred there appeared a prominent Q wave and a sharply inverted T complex clearly indicating the posterior infarct The post extrasystolic pause apparently permitted the specialized conduction tissues to recover from the previous impulse somewhat more completely than did the usual interval between beats This case illustrates how left bundle branch block tends to obscure the evidence of infarction

Myocardial Infarction Complicated by Arborization Block

Defects in intraventricular conduction other than right or left bundle branch block do occur in myocardial infarction As a rule such defects do not abolish abnormally large Q or QS deflections because they do not affect the initial negativity of the left ventricular cavity Delayed intraventricular conduction of this type may be due to a functional depression of the specialized conducting system or of the ventricular musculature as a whole, to lesions involving one or more of the subdivisions of the bundle branches or to involvement of the Purkinje network or subendocardial muscle in the region of the infarct itself The name arborization block was given conduction defects of the latter type by Oppenheimer and Rothschild[11] although the criteria they proposed must be modified today

The electrocardiograms reproduced in Fig 73 are those of a man aged 46 who had a myocardial infarction on August 6 1941 after having hypertension for nine years The records shown were taken on May 5 1942 but others made one month after the acute coronary thrombosis were very similar The limb leads display a QRS interval of 0 14 sec deep Q waves in leads II III and V_F and broad S deflections in lead I These records resemble those shown in Fig 71 and posterior

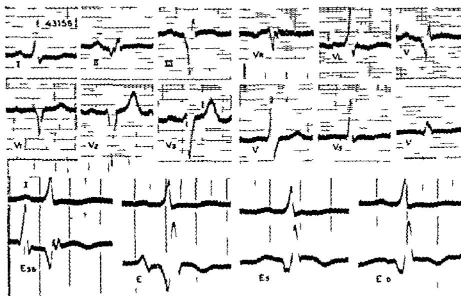


Fig 73 Posterior myocardial infarction complicated by arborization block The limb leads show a QRS interval of 0 14 sec and prominent Q waves in leads II III and V_F and small S waves in lead I These changes suggest posterior myocardial infarction plus right bundle branch block but the precordial leads fail to confirm the latter Leads E_{46} and E_{50} from the ventricular levels of the esophagus show prominent Q waves indicating the lesion of the posterior ventricular wall and large late R deflections due probably to delayed activation of less seriously involved muscle overlying the infarcted zone This man, aged 46 years had symptoms of myocardial infarction nine months earlier Electrocardiograms at that time were similar to those reproduced here except for transient T wave changes (From an article by Wilson and associates[9])

infarction complicated by right bundle branch block was suspected The precordial electrocardiograms show no late R deflections in leads V_1 or V_2 and the diagnosis of right branch block was not sustained Leads from the ventricular level of the esophagus E_{46} E_{50} and E_{60} display

large broad Q waves and tall late R deflections These changes suggest that the infarct involved the subendocardial muscle or Purkinje plexus on the inner aspect of the affected region on the posterior wall of the heart thereby producing a local delay in conduction as well as permitting the initial negativity of the left ventricular cavity to be transmitted to the epicardial surface during the first part of the QRS interval The delayed activation of the less seriously involved outer layers of ventricular muscle was probably responsible for the large late R deflection

Value of Electrocardiogram in Management of Patients with Acute Myocardial Infarction

The primary value of the electrocardiogram in the management of patients with acute myocardial infarction is in establishing the diagnosis Electrocardiographic studies are of limited or indirect value in observing the progress or estimating the prognosis in any given case If a patient has only minor constitutional manifestations and the electrocardiographic changes are confined to the T waves alone or to the QRS and T complexes of only one or two of the precordial leads it may be presumed that the infarcted area in the myocardium is relatively small Such patients seem to do well probably because for the most part the smaller the involved zone the better the outlook for that particular attack On the other hand it is not uncommon to see patients develop congestive heart failure pneumonia peripheral emboli or other serious complications of acute coronary thrombosis while the electrocardiograms are following the usual retrogression to a more normal outline The physician must use the electrocardiogram only as another laboratory approach to his clinical problem Graphic records do not help him to anticipate the serious complications of this disorder If the clinical findings make the physician suspect the development of a significant arrhythmia or extension of the original zone of infarction the electrocardiogram may give him useful information Once the diagnosis of myocardial infarction has been established the observations which can be made at the bedside, usually are the best guide to the treatment and management of the patient

Miscellaneous Disorders Which Alter the Form of the Electrocardiogram

There are a great many clinical disorders other than myocardial infarction which affect the configuration of the electrocardiogram, particularly the outline of the ventricular complex. Some of these disturbances produce electrocardiographic changes which are sufficiently characteristic to suggest rather strongly to the observer that a certain situation is present: tracings made during an attack of angina pectoris or records from patients with pulmonary infarction or acute pericarditis may show alterations quite peculiar to those disorders. There are many diseases which give rise to less distinctive changes in the electrocardiograms. Sprague[11] compiled a list of forty conditions other than coronary atherosclerosis which may alter the S-T segments and T waves. Because there is little in the electrocardiograms in these disorders to distinguish one from the other, etiological diagnoses are to be avoided in interpreting such records. Electrocardiographic observations in diseases such as myxedema, beri-beri, trichinosis, severe infections and toxemias serve primarily to support or amplify the clinical diagnosis. As indicated, either etiological or pathological diagnoses can be made only rarely from the electrocardiogram. The coronary arteries themselves influence the electrocardiogram directly only as they control the myocardial blood supply. It is erroneous to use the phrases "coronary sclerosis," "coronary narrowing," "coronary T waves," or other similar terms in electrocardiographic interpretation because the changes referred to may actually be the result of one of a multitude of quite different diseases affecting the myocardium directly.

Angina Pectoris

Transient changes of considerable significance may be observed in electrocardiograms recorded during spontaneous or induced attacks of angina pectoris. Alterations of this type are the basis for the exercise test employed by Master[247] and Riseman[248] and the anoxemia test devised by Levy[249]. The physician frequently is confronted by the necessity for proving or disproving the diagnosis of angina pectoris in patients presenting neither objective clinical findings nor abnormalities in the electrocardiogram recorded at rest. If distinctive electrocardiographic changes can be recorded during a spontaneous or induced attack of

cardiac pain the diagnosis is strongly supported Failure to record such changes does not exclude the diagnosis but it does lead the clinician to search carefully for other possible causes for the pain The changes consist primarily of displacement of the RS T segments in leads II and III or in all the standard leads Prominent S deflections often appear in leads II and III and the T waves may become inverted usually in those leads showing the least displacement of the RS-T segment There is commonly reversal of the direction of the T waves in the precordial leads[1] a feature which Alzamora recently emphasized[1 1] This observer found that patients whose resting electrocardiograms show sharply inverted T waves in the precordial leads do not develop still more abnormal records during period of stress as might be anticipated but instead the T complexes become upright although often pointed notched or otherwise peculiar in form The criteria to be used in evaluating electrocardiographic changes during anoxemia or exercise tests have not been finally established[1] Occasionally the changes in the electrocardiogram during an attack of angina pectoris are comparable in magnitude and similar in kind to those produced by a major coronary occlusion[1 1] but differ in that they are very transient and do not show the subsequent progressive changes which follow infarction Some patients with angina pectoris may show definite electrocardiographic changes during smoking[1 4 1 3], or after eating[1 1], even though no pain is present at the time

The electrocardiograms reproduced in Fig 74 are those of a physician aged 66 years who developed angina pectoris two months before these observations were made The pain was unusual in that it radiated not only to the arms but also to the neck teeth head and as low as the waistline Low grade hypertension had been present for many years The examination was negative except for a blood pressure of 160/98 mm Hg The initial tracing is abnormal because of slight left axis deviation slightly inverted T waves in lead I and slight flattening of the RS-T segments in leads II and III Immediately after this record was made a spontaneous attack of cardiac pain occurred The curve taken at the peak of this attack (second row Fig 74) shows pronounced depression of the RS T junction and segment in leads II and III the development of an S deflection in lead II and an increase in the size of the S deflection in lead III The pain was relieved after nitroglycerine was given and the electrocardiogram gradually returned to its resting form The patient died suddenly one week after these studies were made Bryant[154] has observed a patient who showed similar changes in

the standard leads and upward RS T displacement in the precordial leads one day later an anterior myocardial infarction occurred with typical electrocardiographic abnormalities Such a sequence suggests that the original changes were the result of ischemia of that part of the myocardium supplied by the left anterior descending coronary artery Other cases of this type have shown elevation of the RS-T segments in

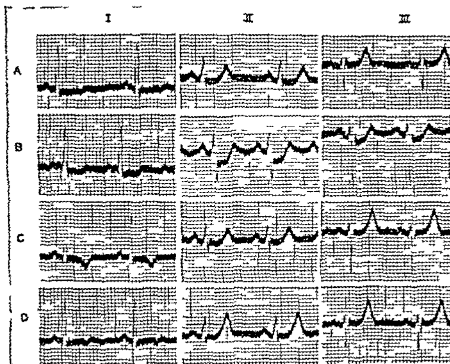


Fig 14 Angina pectoris A Control electrocardiogram shows slight left axis deviation and slightly inverted T waves in lead I B Record made at the peak of a spontaneous attack. Note pronounced depression of RS T junction and segment in leads II and III appearance of S deflection in lead II and increased size of S in lead III C. Five minutes after B following administration of nitroglycerin gr 1/100 changes are less pronounced D Ten minutes after C record is now similar to control The patient aged 60 years had low grade hypertension for many years and angina pectoris for two months He died suddenly one week after these studies were made (From an article by Wilson and Johnston[13])

leads II and III and depression of the RS T segment in lead I, in such instances the ischemia probably is in the posteroseptal subepicardial region of the left ventricle supplied by the right coronary artery[13]

The ischemia responsible for the electrocardiographic abnormalities associated with angina pectoris is believed to be due in part to changes in the caliber of the coronary arteries and arterioles and probably in part also to increase in the work of the heart.

Pulmonary Embolism

Recent developments in the management of patients with acute pulmonary thrombo-embolic disease, particularly venous ligation and anti-coagulant therapy, make it important that the diagnosis be made promptly and accurately. The electrocardiogram may give useful information in patients with pulmonary infarction, particularly in differentiating this disorder from acute myocardial infarction. The electrocardiographic pattern in pulmonary embolism as described in the literature has been variable[104, 155, 156, 157, 158, 159], and the configuration of the records does seem to differ from patient to patient. There are probably several factors which contribute to these variations, including the extent of the infarction, the time at which the observation is made after the embolus lodges in the lung, the co-existing disease — especially cardiac disease — and the medication the patient is receiving. The most consistent electrocardiographic change in acute pulmonary embolism is inversion of the T waves in records taken from the right precordial zone[160, 161]. This inversion appears earliest, is most marked and is of greatest duration in leads V_1 and V_2. Inverted T waves may occur in all the precordial leads, but they tend to become upright as time passes, and those over the left precordium become normal earliest. Prominent S deflections in leads I and V_L, small late R waves in leads III and V_R, prominent Q waves in lead III, and depression of the RS-T junction with stepwise ascending RS-T segments in leads I and II are also observed commonly. Complete or incomplete right bundle branch block occurs in some cases, but when prominent S deflections appear in lead I in these patients, delayed activation of the right ventricle is not always present[161]. All of the findings are transient, and their relatively short duration is of especial interest. The electrocardiographic changes attending pulmonary infarction usually clear in 7 days to three weeks, whereas those resulting from myocardial infarction last many weeks or months. The abnormalities associated with pulmonary infarction are usually fully developed in 2 to 24 hours; the alterations produced by myocardial infarction are usually most striking only after several days have elapsed.

The records shown in Fig 75 are those of a woman aged 39 years who had an hysterectomy and appendectomy on May 6 1944 Eleven days later she complained of pain in the left thigh and on the evening of the following day she had a sudden attack of chest pain accompanied by faintness dyspnea and shock The first electrocardiogram in Fig 75 was taken one hour and forty five minutes later and the second was recorded twenty two hours after the attack The patient died four hours after the second tracing was made The post mortem examination showed massive pulmonary embolism with all the larger pulmonary arteries stuffed with emboli and blood clots pulmonary arteriosclerosis

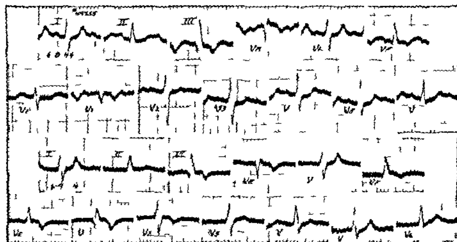


Fig 75 Pulmonary embolism June 8 1944 the limb leads show prominent S waves slight depression of the RS T junction and staircase ascending RS T segments in leads I and V. There are prominent Q waves and inverted T waves in lead III The precordial leads show only a peculiar sharp angulation of the ascending limb of the T waves in leads V V V and V June 9 1944 the limb leads now show auricular fibrillation but otherwise they are unchanged The precordial leads show prominent late R peaks in leads V and V suggesting incomplete right bundle branch block and sharply inverted T waves in leads V V and V such as are common at these points in pulmonary infarction This woman aged 39 years had an hysterectomy and appendectomy on May 26 1944 She died four hours after the second record was taken Postmortem examination disclosed massive embolism of all the larger pulmonary arteries (From an article by Wilson and associates [6])

with organizing and recanalized thrombi a few areas of active pulmonary arteritis and a normal heart The two sets of limb leads are quite similar Prominent S waves slight depression of the RS T junction and staircase

ascending RS T segments are seen in leads I and V_1 Prominent Q waves and sharply inverted T waves are present in leads III Small late R deflections are present in lead V_1 In the second set of records the QRS interval is slightly longer and auricular fibrillation is present The initial set of precordial electrocardiograms shows sharp inversion of the T waves in lead V_1 and slight depression of the RS-T segment with sharp angulation of the ascending limb of the T complex in leads V_3 V_4 V_5 and V_6 The precordial leads on the following day are quite different in that they show prominent late R waves in leads V_1 and V_2 suggesting incomplete right branch block and sharply inverted T waves in leads V_1 V_2 and V_3 This case is of particular interest because at the time of the initial observation prominent S waves were present in lead I, a frequent transient phenomenon in pulmonary infarction in the absence of any demonstrable intraventricular conduction defect This particular change probably is due to an unusual rotation or shift in the position of the heart in the chest[161] The other electrocardiographic changes in pulmonary infarction have been attributed to right ventricular myocardial ischemia resulting from increased right ventricular pressure decreased aortic pressure and consequent diminished flow to the right ventricle through the coronary thebesian circuit Despite this reduced flow the right ventricle is called upon to perform more work than is normal

Digitalis

Digitalis produces rather characteristic changes in the RS T segment and junction and the T waves[1, 163] (Figs 764 b c, d) When digitalis is given to a patient the earliest change is depression of the RS T segments in both the standard and precordial leads especially those in which the chief QRS deflection is large and upright As digitalization progresses this depression of the RS-T segment increases and the RS T junction becomes displaced below the iso electric level Further digitalization causes inversion of the initial portion of the T wave and since the final portion of this complex remains upright the entire deflection then is diphasic Ultimately the T wave becomes entirely inverted and U-shaped The progressive inversion of the T wave which occurs with digitalis proceeds from the initial portion of this deflection toward its end whereas the progressive change in this complex produced by myocardial infarction proceeds from the terminal portion toward its beginning or ascending limb These abnormalities of the RS-T segment and T

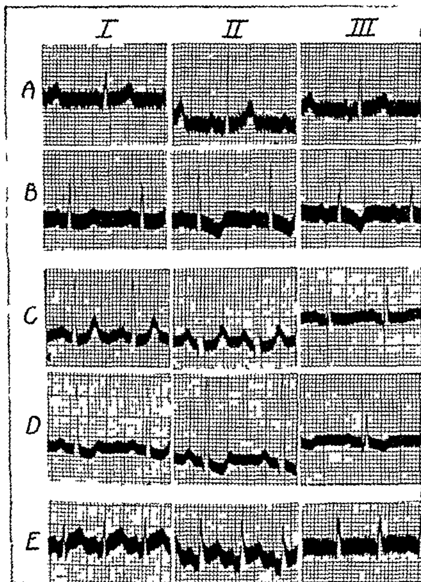


Fig. 76 Digitalis A and B the standard leads taken before treatment are normal (A) but after digitalis was given in full doses the T waves are inverted and L haped in leads II and III (B) C and D the standard leads of a second patient before (C) and after (D) administration of large doses of digitalis Note the inversion of the early portion of the RS-T segment and T waves in all leads

Acute pericarditis (E) There is distinct upward displacement of the RS-T segment in all leads but particularly in leads I and II The QRS complexes are of rather low amplitude but otherwise are normal This patient had an acute purulent pericarditis (From an article by F N Wilson[144])

waves usually cannot be considered evidence of digitalis intoxication, but when present, they are important because they may indicate that a patient, unable to give an adequate history of his previous treatment has already received digitalis. The electrocardiographic changes which are more significant so far as serious digitalis intoxication is concerned include the various degrees of atrioventricular block, extrasystolic bigeminy, extrasystoles arising from multiple foci and idioventricular rhythm. Clinical observations usually are far more important than electrocardiograms in regulating digitalis dosage but occasionally patients may develop one of these serious disturbances without the usual gastrointestinal, visual or mental manifestations of over digitalization. Electrocardiographic observations have been useful in the bioassay of some of the digitalis glycosides[164]. Two or three weeks are required for the electrocardiographic effects of the drug to clear after digitalis has been discontinued.

Pericarditis

Acute pericarditis, no matter what its etiology, very commonly produces distinctive electrocardiographic changes[165, 166, 167, 168, 169]. The electrocardiographic changes may be present even when no friction rub is heard. The most characteristic change is elevation of the RS-T segment in leads I and II, leads II and III or in all the standard leads and in the precordial leads (Fig. 76(e)). The displacement of the RS-T segment which occurs in pericarditis is concordant, i.e., in the same direction in all the standard leads, whereas that seen in myocardial infarction is discordant, i.e., in opposite directions in leads I and III. During the stage of pericarditis when the displacement of the RS-T segment is maximal, the ascending limb of the RS-T segment often is concave or ascends in a straight line and the T waves tend to be exaggerated and sharp[166]. The displacement of the RS-T segment is transitory and as it declines there appears progressive inversion of the terminal portion of the T waves in those leads which originally showed RS-T displacement. This usually occurs within one to three weeks from the onset of the disease. There is a transitional period when the RS-T displacement is clearing and T wave inversion is not well developed, during which the tracings may appear nearly normal. In such instances additional observations must be made after a few days to demonstrate the further changes in the T complexes. The inverted T waves in acute pericarditis strongly

resemble those produced by myocardial infarction with the exception that usually they are not as deep Acute pericarditis is not associated with significant modifications of the QRS complexes unless it complicates myocardial infarction If the acute pericarditis subsides the electrocardiograms become normal within one to three months

The electrocardiographic changes of acute pericarditis have been attributed to subepicardial myocarditis[1] Bayley and LaDue[2] expressed the opinion that the electrical effects associated with experimental postoperative pericarditis are generated by the muscle adjacent to the local epicarditis Clinical acute pericarditis is usually a diffuse process because of this the effects of acute myocardial ischemia and injury are recorded from large areas over the heart and consequently appear usually in all or nearly all of the standard and precordial leads

Chronic pericarditis or chronic constrictive pericarditis usually is accompanied by electrocardiograms which display QRS complexes and T waves which are of low amplitude in all of the standard leads[1] The T waves may be inverted in one or more of the standard leads and often in the records taken from the left precordial area Auricular fibrillation is observed commonly in chronic constrictive pericarditis one of several features which tend to make these cases confused with rheumatic heart disease with mitral stenosis

Low Voltage Slurring and Notching of the QRS Complexes

Electrocardiograms in which the QRS complexes show abnormally small amplitude or slurring or notching of the deflections occur in a great variety of conditions and it is necessary that such tracings be evaluated with care So many serious errors occur from placing too much emphasis upon minor changes of this nature that it is well to give considerable thought to the possible origin of these abnormalities and the clinical picture presented by the individual being considered

The term low voltage or low amplitude is used to designate those electrocardiograms in which the largest deflection of the QRS complex in any of the standard leads is 5 mm or less above or below the base line Early studies suggested that low voltage is a very serious sign[1,2,3] but more recent observations indicate that this is not necessarily the case Lapin[113] recently has summarized the data from eight reports concerning the electrocardiograms of 5 673 healthy persons and found that low voltage occurred in the standard leads in 1 3 per cent of these individuals

Wilson[7 1] has pointed out three general conditions which may result in QRS deflections of low amplitude (1) There are disorders which tend to reduce the total electromotive forces developed by the myocardium by actually reducing the mass of muscle activated by each cardiac impulse such as may occur in myocardial infarction or arteriosclerotic heart disease with extensive myocardial fibrosis (2) Some conditions alter the conductivity of the tissues surrounding the heart Accumulation of fluid about the heart or in the body tissues may produce low voltage by the increased short circuiting effect which the increased amount of conducting extracellular medium has upon the cardiac currents this occurs in anasarca pleural effusion ascites and pericardial effusion Low voltage may result from the insulating effect of a layer of air around the heart as in pneumopericardium or emphysema (3) Several factors such as the position of the heart the contour and symmetry of the thorax and the thickness of the chest will also may influence the size of the deflections If the position of the mean electrical axis is perpendicular to the frontal plane of the thorax low voltage tends to appear in the standard leads and the records from the left precordium In general it may be said that if there is no other evidence of disease either clinical or electrocardiographic and the QRS deflections are of normal outline except for the amplitude low voltage can be disregarded

Lapin[13] has made a recent study of low voltage in the precordial leads He used the criteria of 0 9 mv or less in leads V V_3 V_4 and V_5 and 0 7 mv or less in lead V_6 Of 100 patients who had low voltage in the standard leads 65 had low voltage in the precordial leads It was his impression that the same electrophysiological factors operate to produce low voltage in the precordial leads as in the standard leads The vast majority of the patients who have low voltage in both the standard and precordial leads had serious heart disease but in a few instances there was *no* organic disease of any kind Such cases were considered to represent an unusual orientation of the mean electrical axis Low voltage was uncommon in all of the precordial leads Lapin pointed out that when the standard leads are small precordial leads V and V_6 also tend to be small since they too arise from forces operating in the frontal plane Furthermore in some of these cases forces acting in the sagittal plane may give rise to large deflections in precordial leads V and V_3 but have little effect upon the standard leads or leads V and V_6

More important than the size of the QRS complex is its configuration If the deflections in all the limb leads are small and bizarre, myocardial infarction or bundle branch block is quite apt to be present (Fig 70)

In many of these patients the QRS deflections of the precordial leads are of normal size or even abnormally large even though those of the limb leads are abnormally small The mean electrical axis is quite probably perpendicular to the frontal plane throughout most of the QRS interval in such cases

The term slurring is used to designate those records in which the slope of the deflection becomes less abrupt with a resultant thickening or widening of the trace Notching is as the name implies a sharp temporary reversal of direction of movement of the trace When these particular changes are confined to those leads in which the QRS deflections are small they usually have no great significance Slurring or notching which occurs near the iso electric level is common in normal curves and also is of doubtful significance Such changes usually result from the combination of potential variations of opposite kinds derived from two different parts of the heart s surface and occurring out of phase i e at slightly different times It is common to see striking notching in the precordial leads taken from the transitional zone usually leads V V₃ or V₄ Such notching is the result of the admixture of potential variations such as occur to the right of the transitional zone with potential variations such as occur to the left of that point Notching which has this origin usually is of no clinical significance On the other hand when the QRS complexes of all leads are notched or slurred and this change occurs at the apex of large deflections the records are probably abnormal Notching of this type occurs in bundle branch block as the result of incomplete fusion of that part of the R wave which arises from the spread of the wave of activation through the septum and that portion of the R wave which arises from the activation of free wall of the ventricle on the side of the lesion Although such notching may represent some conduction disturbance it usually is not of diagnostic significance unless the QRS interval is also prolonged

Myxedema

Myxedema causes definite although rather non specific electro cardiographic changes All of the deflections are reduced in amplitude and the T waves become flattened or even inverted The heart rate tends to be slow and the P R interval may be slightly prolonged The degree of change from the normal is roughly proportional to the severity of the hypothyroidism After treatment there is progressive return of the

tracings toward the normal pattern The changes which occur in this disorder have been described well by Tung[174] and the records shown in Fig 77 are from one of his cases This patient was a woman aged 51,

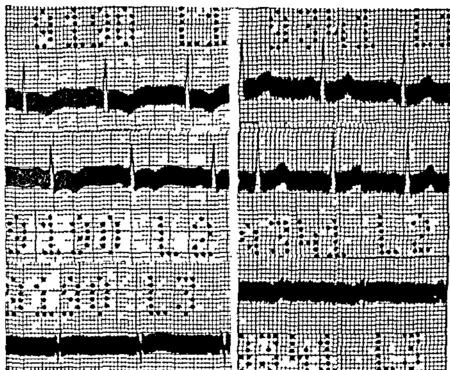


Fig 77 Myxedema Record 9190 The standard leads before treatment the basal metabolic rate was minus 36 The QRS complexes are of rather small amplitude and the T waves are inverted in leads I and II Record 9341 The standard leads after thyroid treatment the basal metabolic rate was plus 8 The QRS complexes are larger and the T waves have become normal (From an article by Tung[174])

whose basal metabolic rate was −36 before treatment was begun The records taken at that time show inverted T waves in leads I and II and rather small QRS deflections in all leads Nearly one month later when the basal metabolic rate had risen after thyroid therapy to plus 8 the electrocardiogram was entirely normal It is well to remember as Christian[175], Smyth[176] and others have emphasized that desiccated thyroid must be administered cautiously to patients with angina pectoris lest the cardiac pain be aggravated or actual *myocardial infarction* be precipitated

Acute Myocarditis

Any type of acute infectious or toxic disorder which affects the heart may modify the electrocardiogram The changes produced usually are confined to the T waves or RS T segments but if the specialized conduction tissues are involved also prolongation of the P R interval intraventricular block or disturbances in rhythm may occur The changes usually are transient clearing as the acute process subsides but if myocardial scarring or fibrosis of sufficient extent occurs the alterations may be permanent The electrocardiograms may be of some help in managing these patients for as long as the electrocardiographic changes are *progressing or regressing the acute process would appear to be active* and the heart should be kept at rest Once the electrocardio graphic changes become stationary the records may be disregarded so *far as regulation of the patient s activity is concerned*

Diphtheria may involve the myocardium quite extensively Myocarditis occurs especially in severe faucial or cutaneous diphtheria particularly if there is associated peripheral neuritis[1 2] Inversion of the T waves in one or more of the standard leads has been the most common finding reported but Hill recently has pointed out that depression of the RS T segment nearly always precedes the inversion of the T waves Burkhardt and his associates observed changes in the T waves in 3 of 140 cases of faucial diphtheria the abnormalities appearing chiefly during the second and third weeks of the disease Seventeen patients in this group developed defects in conduction and fourteen fatalities occurred The changes associated with diphtheria usually clear completely but rare instances of permanent heart block following this disease have been recorded[3]

An example of the acute myocarditis which may complicate scarlet fever[42] is shown in Fig 78 This patient was a boy aged , years whose symptoms began on January 1 194 The course was mild and uncom plicated for three weeks whereupon he developed increasing edema and dyspnea On February 1 the blood pressure was 140/1 0 mm Hg the heart was enlarged and a gallop rhythm appeared There was also evi dence of an acute glomerular nephritis Electrocardiograms taken at this time show slightly inverted T waves in leads I and V1 All evidence of myocardial and renal involvement cleared rapidly and the second set of tracings taken on March 9 194- show normal T waves and some increase in the amplitude of the QRS deflections in all leads It is quite possible that the myocarditis and the electrocardiographic changes observed in

this case were produced by the acute glomerulonephritis much as in the instances reported by LaDue and Ashman[18], Langendorf and Pick[13] and others

Gore and Saphir[191] recently have reviewed 1,402 cases of myocarditis verified by pathological examination More than 50 different disorders were responsible and more than 90 per cent of the cases were non rheumatic in origin The known etiological agents cited in this particular report and in other similar ones have included drugs and toxic substances (insulin arsenicals sulfonamides antimony emetine) physical agents (heat and cold) various virus rickettsial spirochetal fungus and



Fig 8 Acute myocarditis associated with scarlet fever February 13 194 the limb leads show slightly inverted T waves in leads I and VF and abnormally flat T waves in lead II March 9 194 the QRS deflections now are larger and the T waves are of normal contour This boy aged 7 years developed scarlet fever on January 1 194 Edema dyspnea hypertension pulmonary congestion and cardiac enlargement began three weeks later There was also evidence of acute nephritis Rapid improvement occurred and all the abnormal signs had cleared when the second records were taken

parasitic diseases less specific infectious diseases and disorders of nutrition or metabolism In the series of Gore and Saphir[191] the electrocardiograms showed evidence of myocardial damage in the majority of instances in which observations were made For the most part disturbances of this type produce *inversion of the T waves in one or more leads* less commonly changes in the RS T segment or prolongation of the P R interval Only rarely are there significant changes in the QRS complexes The electrocardiogram in myocarditis of these varieties serves primarily to confirm the clinical impression that the disease has involved the myocardium and thereby to substantiate the diagnosis The electrocardiographic changes usually are transient and not particularly characteristic in configuration

Circulatory and Emotional Instability

The electrocardiograms of a portion of those patients with emotional or circulatory instability have been found to show variations in the configuration of the T waves including inverted T waves in leads II and III and flat or slightly inverted T waves in lead I. These patients have no other evidence of heart disease. Logue and his associates[58] reported electrocardiographic variations of some form in nearly one half of 150 cases classified as neurocirculatory asthenia. In some instances the T waves become inverted in one or more of the standard leads only after the patient assumes the upright position. It is not yet clear whether alterations of this type which occur on assuming the erect position are due to changes in the position of the heart or to reflex discharge of sympathetic stimuli. Wendkos[9] has observed emotionally unstable patients whose records showed inverted T waves in the leads from the left sternal margin. In some instances the tracings became normal on standing or after amyl nitrite or atropine, whereas ergotamine caused the changes to reappear. In other cases the response to these procedures was quite the reverse. It would seem therefore that variations of the T waves in the precordial leads may result from a preponderance of either vagal or sympathetic tone. Such variations may occur in the absence of structural heart disease but may simulate T wave alterations produced by various myocardial disorders. A study of the responses to changes in positions and to drugs such as atropine, amyl nitrite and ergotamine may help to evaluate changes in the T waves in the standard and precordial leads when emotional or circulatory instability is suggested by the clinical findings[139].

Changes in Serum Potassium Concentration

Certain electrocardiographic abnormalities accompanying clinical disorders in which the electrolyte balance is disturbed have been found recently to be due to alterations in the serum potassium concentration[6, 8, 99, 10, 11]. These abnormalities have been seen to disappear when the serum potassium level returns to normal.

Abnormal elevations of the serum potassium concentration occur in severe renal insufficiency and in disorders in which potassium salts are used as diuretics or alkalinizing agents, or in the treatment of cardiac irregularities or digitalis intoxication. The earliest electrocardiographic

change associated with hyperkaliemia usually is an increase in the height of the T waves so that they appear tall and peaked with a narrow base This change usually occurs in the standard leads and may be seen also in the precordial leads It has been reported that the T waves may become inverted in the precordial leads but in these reports the actual records may have been influenced by the potential variations of the extremity used for the reference electrode Subsequent changes which develop as the serum potassium level rises include prolongation of the P R interval intraventricular block reduction in the size of the P waves with ultimate auricular standstill complete heart block and finally gradual cardiac slowing with terminal cardiac standstill The QT interval usually is unaltered Although there is considerable individual variation it appears that the electrocardiogram is unchanged so long as the serum potassium level is below 6 8 mEq /L abnormalities may appear when the concentration is between 6 8 and 7 6 mEq /L and they are recorded almost regularly when the level is greater than 7 8 mEq /L [10] An example of quite profound electrocardiographic disturbances occurring in a patient with malignant hypertension is illustrated in Fig 78a These observations were made when the serum potassium level was 8 5 mEq /L When such abnormalities are recorded in the electrocardiogram it has been recommended that the patient be given hypertonic glucose and physiological saline solutions intravenously Such treatment must of course be considered in the light of the entire individual clinical problem

Abnormal reduction of the serum potassium concentration is associated with several clinical disorders including familial periodic paralysis intestional obstruction desoxycorticosterone acetate intoxication and diabetic acidosis It has been observed that in diabetic acidosis the serum potassium concentration is elevated initially but that it becomes reduced to abnormally low levels after treatment with insulin has been started [11] The electrocardiogram in hypopotassemia is characteristic by depression of the RS-T segment prolongation of the QT interval and at times lengthening of the P R interval The T waves usually are reduced in amplitude or actually they may become inverted Nadler and his associates [11] pointed out that the prolongation of the QT interval in hypocalcemia is due to prolongation of the isoelectric period between the end of the QRS complex and the beginning of the T wave whereas the prolongation of the QT interval in hypopotassemia is the result of widening of the T wave itself These workers recommended inspection of precordial leads rather than the standard leads for this particular type of

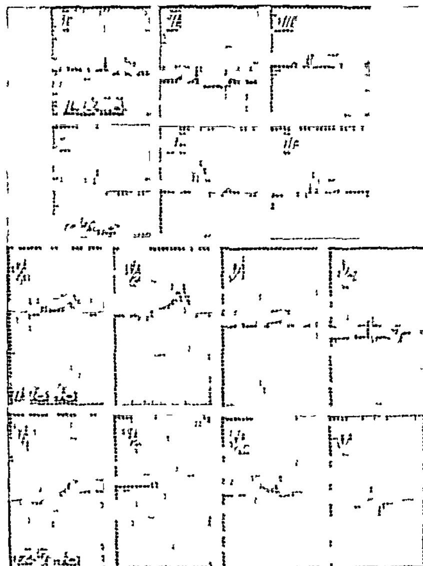


Fig 78a Abnormal elevation of the serum potassium concentration On Nov 17 1948 the serum potassium concentration was 3 2 mEq/L The serum calcium level was 10 3 mgm per cent and the blood urea nitrogen concentration was 69 5 mgm per cent The earliest electrocardiograms shown were recorded on the following day They show inverted T waves in lead I II and V suggesting myocardial changes On Dec 6 1948 the serum potassium concentration was 8 5 mEq/L the serum calcium level was 9 mgm per cent and the blood non protein nitrogen concentration was 333 mgm per cent The second set of tracings was taken on the following day These records show intraventricular block and probable auricular standstill No p waves are present in leads V and V where usually they are quite prominent This man aged 35 years had malignant hypertension He died a few hours after the second electrocardiograms were made (Courtesy of Dr F D Murphy and Dr T R Murphy)

change Hypopotassemia may be treated by administration of an isotonic solution of potassium chloride intravenously

Although electrocardiographic observations cannot be considered a substitute for chemical determinations of serum potassium levels, they do add to our understanding of the pathological physiology of these serious affections of electrolyte metabolism and particularly in diabetic acidosis and renal disorders they may be a useful guide to proper treatment of the patient

Congenital Heart Disease

Interest in the more exact anatomic diagnosis of congenital heart disease has been stimulated in recent years by the introduction of surgical procedures for the correction or alleviation of patent ductus arteriosus coarctation of the aorta vascular ring and the tetralogy of Fallot The electrocardiogram gives useful supplementary information to the clinician studying a case of congenital heart disease and in some instances findings of particular interest are recorded[18, 148, 183] The increased interest in these problems and the use of multiple precordial leads and other special leading undoubtedly will augment our present knowledge

Quite specific findings may be present in the electrocardiograms of certain cases of congenital heart disease Congenital complete heart block may be diagnosed with certainty by graphic methods In contrast with the older cases of arteriosclerotic origin this type of complete heart block is less constant in its rate and more labile in response to exercise or sympathomimetic drugs so that it may be confused with sinus bradycardia with sinus arrhythmia unless electrocardiograms are taken True dextrocardia produces a very distinctive picture, in which all of the major deflections are inverted in lead I and leads II and III appear interchanged (Fig 79) This same type of record is produced, if the lead wires from the right and left arms are interchanged inadvertently so that an artifact of this type always must be excluded When left axis deviation and electrocardiographic evidence of left ventricular hypertrophy occurs in a patient with cyanosis tricuspid atresia and gross underdevelopment of the right ventricle is strongly suggested[178, 183]

The electrocardiographic signs of right ventricular hypertrophy are commonly associated with those forms of congenital heart disease which are accompanied by persistent cyanosis As has been pointed out right axis deviation usually is present in the standard leads in these patients

but it may fail to appear if the heart is vertically or semi vertically placed The configuration of the precordial leads is a more reliable index of the type of hypertrophy in such cases Right ventricular hypertrophy also occurs in some patients with auricular septal defects Lutembacher s syndrome and pulmonary stenosis with a closed interventricular septum Left ventricular hypertrophy is less common in congenital heart disease It occurs in some instances of coarctation of the aorta and subaortic stenosis Lesions which produce an additional load upon both the right

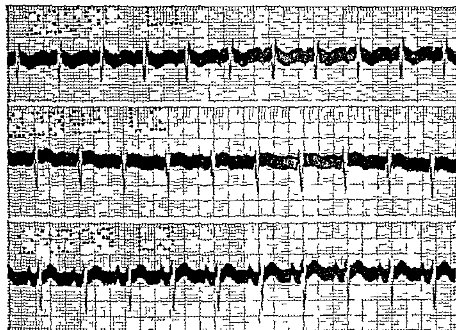


Fig 79 Dextrocardia The P waves the major deflect n in the QRS complex and the T waves are all directed downward in lead I This rec rd w uld appear more normal if lead I were turned upside dov n an l lead II and III were interchanged This boy aged 12 years had pulmonary tuberculosi In additi n to dextrocardia there was complete situs inversus viscerum

and left ventricles usually do not affect the electrocardiogram in any striking fashion Uncomplicated cases of patent ductus arteriosus or interventricular septal defect fall into this category

Disturbances of intraventricular conduction especially complete or incomplete right bundle branch block may be observed in some patients

with a defect in the interventricular septum presumably because the lesion or its sclerotic margin has interrupted one or more of the specialized conduction pathways Complete heart block also may occur in these patients On the other hand, ventricular septal defects may produce no significant electrocardiographic changes or bizarre, broad QRS complexes may be present even though the ventricular septum is intact Taussig[188] has found that widened QRS complexes are more common in auricular than in ventricular septal defects

Alterations in the outline of the T waves may occur in those anomalies which produce persistent cyanosis in which venous blood courses through the coronary arteries Quite striking changes have been reported in those instances in which one of the coronary arteries arises from the pulmonary artery instead of the aorta[190, 191] In one such case *the clinical and electrocardiographic picture simulated an acute coronary* thrombosis[110] Inversion of the T waves in records from the right precordium and even to the third or fourth position often is difficult to evaluate in children suspected of having congenital heart disease because this deflection is often inverted in normal children[10] whereas in normal adults the T waves are upright in all of the standard precordial leads except lead V1

Anomalous Atrioventricular Excitation (Wolff-Parkinson-White Syndrome)

There is a curious cardiac anomaly characterized primarily by *electrocardiograms which show a P R interval which is abnormally short* and a QRS interval which is abnormally long[19] A high percentage of the patients exhibiting such records have paroxysmal tachycardia either auricular nodal or less commonly ventricular and a few have shown paroxysmal auricular fibrillation or flutter The majority of these patients have no other evidence of heart disease and in many instances the abnormality has been discovered accidentally Other cases have shown signs of heart disease in addition to the electrocardiographic changes[193, 194] Reversion of the anomalous electrocardiogram to records of normal form may occur spontaneously or after exertion amyl nitrite *atropine or quinidine It has been considered generally that this condition* is benign but with it a few instances of sudden death or death during paroxysmal tachycardia have been reported[111, 193, 19, 196, 19] Many hypotheses have been advanced to explain this peculiar disorder but the

one which best satisfies the various phenomena which have been observed postulates that the auricular impulse reaches the ventricles by one or more accessory pathways in addition to the bundle of His[98, 1]. Accessory atrioventricular muscular bridges have been described in autopsied cases by Wood and associates[1], Ohnell[1] and Kimball and Burch[19], although somewhat similar bridges have been reported in supposedly normal hearts. It is because of the anomalous spread of the excitation wave that we have preferred the more descriptive term anomalous atrioventricular excitation to the widely used designation Wolff-Parkinson-White syndrome.

Cases of anomalous atrioventricular excitation can be divided into two groups on the basis of the form of the electrocardiogram from the right precordial area[1, 3]. In the first group, illustrated in Figs 80 and 81, the QRS complex of leads V_1, V_2 and V_3 is dominated by a large R wave which is notched or broad topped at its peak. The very earliest or premature component of the QRS complex is positive and shows a gradual slope which fuses with the ascending limb of the R wave. In the leads from the left precordium these cases exhibit taller, sharper R deflections, but slurring of the premature component of the QRS complexes still is evident. The case illustrated here displayed small Q waves in lead V_6 when a normal mechanism was present; this deflection was replaced by the slurred premature upward component of the R wave when the anomalous mechanism was present.

Those cases which make up the second type of anomalous atrioventricular excitation show QRS complexes in leads V_1, V_2 and V_3 which are dominated by a large negative deflection. The premature component in these cases is negative or diphasic. The records from the left precordium are very similar to those of the first type just described. An example of the second type is shown in Fig 82. Here again there are transitions from a normal mechanism so that electrocardiograms of both the anomalous and normal type in the same individual can be compared.

The electrocardiographic evidence accumulated thus far in these cases suggests that the accessory conduction pathway is located on the posterior or right lateral aspects of the atrioventricular groove and that the spread of the impulse through the ventricular muscle activated prematurely by the anomalous pathway is from the epicardial toward the endocardial aspects of the ventricular wall. The differences in the various types of cases which have been observed with this syndrome are no doubt due to several factors, but chief among them quite probably are

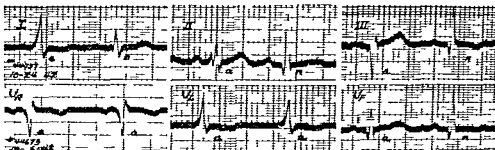


FIG 80 Anomalous atrioventricular excitation (Wolff Parkinson White syndrome) The standard and unipolar limb leads show anomalous (a) and normal (n) complexes When the anomalous mechanism is present the PR interval is 0.10-0.12 seconds and the QRS interval is 0.12 seconds When the normal mechanism is present these intervals become 0.15 sec and 0.07 seconds respectively The slurring of the base of the ascending limb of R in leads I and V is characteristic of this disorder The boy aged 13 years had no other evidence of heart disease (From an article by Rosenbaum and associates[1 4])

FIG 81 Anomalous atrioventricular excitation (Wolff Parkinson White syndrome) The precordial leads V V V V and V E (ensiform and unipolar esophageal leads at four levels show anomalous (a) and normal (n) complexes D_{VIII} is an unipolar lead from the eighth dorsal spinous process In cases of this type the QRS complexes of leads V V and V show large slurred or notched R waves Note the striking slurring of the initial portion of the QRS complex in all leads when the abnormal mechanism is present and the very short P R interval in the esophageal leads at the auricular level (E and E) Same patient as Fig 80 (From an article by Rosenbaum and associates[1 3])

variations in the location and distribution of the accessory pathways and variations in the relative masses of ventricular muscle activated through the normal and the anomalous routes[193, 00, 01] Findings in some instances have indicated the presence of multiple accessory bundles[1 3] and in others all of the ventricular muscle apparently was activated via the anomalous pathway [01]

When cases of anomalous atrioventricular excitation are encountered it is important that they be differentiated from true bundle branch block



Fig 82 Anomalous atrioventricular excitation (Wolff Parkinson White syndrome) Upper row standard leads the first three beats in each record show the normal and the last three the anomalous mechanism Lower two rows the precordial leads the first two cycles in each record show the normal and the last two the abnormal mechanism In all records the upper curve is lead I recorded simultaneously In cases of this type the QRS complexes in leads V V and V are dominated by large negative deflections Records from the left precordium are similar to those of the case illustrated in Fig 81 This man aged 34 years had low grade essential hypertension. The transitions shown were produced in each instance by the Valsalva maneuver (From an article by Rosenbaum and associates[193])

since the underlying defect is quite different The broad QRS interval present in both conditions is the usual source of confusion the unusually

short P-R interval and the characteristic gradual, slurred ascent or descent of the initial portion of the QRS complex in one or more leads should lead to the diagnosis of Wolff-Parkinson-White syndrome when it is present. It should also be realized that paroxysmal rapid heart action occurs in more than half of these cases and although the course usually is very favorable the condition may not be as benign as once was thought to be the case.

The Form of the Auricular Complex

The auricular complex or P wave represents the spread of the activation wave over the auricle. Its direction is normally upward in all leads although occasionally it is diphasic in lead II. The P waves become inverted in leads II and III and unusually flat in lead I, when atrioventricular nodal rhythm occurs (Figs 6 and 8) or when ventricular impulses are conducted in a retrograde fashion through the specialized conduction tissues back to the auricles. The P wave usually is quite smooth or rounded and the maximum amplitude is 1.0 mm in lead I, 2.5 mm in lead II and 2.0 mm in lead III[16].

The outline of the P wave may be altered significantly in certain disorders. In mitral stenosis the auricular complexes tend to become taller than normal, and their duration grows longer than the normal of 0.08 to 0.10 sec. In addition a distinct notch may appear at the peak of the P wave especially in leads II and III. There is some question whether these changes are the result of auricular hypertrophy or of changes in the auricular myocardium. Cases of mitral stenosis with considerable auricular enlargement which are not accompanied by significant alterations in the P waves are seen quite frequently.[9] Patients with congenital heart disease particularly those forms which increase the burden from the auricles commonly have electrocardiograms showing tall peaked P waves without the widening or notching seen in mitral stenosis. Unusually prominent P waves are seen also in patients with hypertensive heart disease, thyrotoxicosis, chronic pulmonary disease, in normal hearts during emotion especially with associated sinus tachycardia and occasionally, in individuals without heart disease.

Large P waves displaying an intrinsic deflection are recorded routinely from auricular levels in the esophagus. This fact may be utilized to study the auricular mechanism in various disturbances of rhythm particularly in those cases in which the P waves are inconspicuous in

the more conventional leads Auricular complexes of similar form in that they too show a distinct abrupt positive to negative shift (intrinsic deflection) may be recorded from the right precordial region in patients with auricular hypertrophy due to rheumatic valvular disease [3] or in situations which bring the right auricle into close apposition with the anterior chest wall [94]

VENTRICULAR GRADIENT

The mean electrical axis of QRS is determined by measuring the areas of the initial ventricular complexes in any two of the three standard leads This axis represents the direction of spread of the excitatory process or depolarization of the ventricular musculature The mean electrical axis of T may be determined in a similar fashion by measuring the areas of the final ventricular complexes in the same leads and it will represent the direction in which the recovery process or repolarization occurs in the ventricle If the duration of electrical systole was equal in all parts of the ventricular musculature that is if all of the individual units of the cardiac muscle passed through the period of excitation in the same interval of time and in the same manner the area of QRS and the area of T would be equal in absolute magnitude but opposite in sign[2] Actually this is rarely the case apparently because of local variations in the excitatory process in various parts of the heart The area of QRS T obtained by the algebraic addition of the area of QRS and the area of T[70] is a measure of the electrical effects produced by these local variations in the excitatory process The mean electrical axis of QRS T determined from the areas of QRS T in two of the three standard levels was shown by Wilson and his associates to give the direction of the line along which these local variations were greatest The vector representing the direction and magnitude of the manifest area of QRS T has been designated the ventricular gradient[11 2]

The difficulties in measurement of the ventricular gradient have restricted its use to some extent Ashman and his associates[112] have developed a method of estimation which they feel is of considerable practical value More exact methods and new instruments are being developed which no doubt will lead to wider use of this type of electrocardiographic study [8] Investigations thus far largely carried out by Ashman and his co-workers[11] and by Bayley[110] have shown that the normal ventricular gradient falls within quite definite limits in its magnitude, direction and relation to the QRS axis The normal gradient is

affected by rotation of the heart about its various axes and by changes in the heart rate the ventricular stroke volume and the patient s posture The gradient is significantly altered in magnitude direction or its relation to the other electrocardiographic axes by anything which alters the state of the cardiac muscle This type of approach promises to be particularly useful in evaluating minor changes in the T waves in the standard leads and in differentiating T wave alterations which are secondary to variations in the configuration of the QRS complexes from those produced by primary myocardial disease It has been shown that changes in the T waves *which are secondary to unusual variations in the position of* the heart are associated with a normal ventricular gradient whereas a gradient which deviates beyond the normal range is present when the abnormalities in the T waves are produced by actual myocardial disease

CONCLUSION

An attempt has been made in the material presented here to give the reader *some understanding of the principles upon which* electrocardiography is based and to indicate the place of this method of study in the clinical practice of cardiology It is proper also that the clinician should be mindful of the limitations of electrocardiography Except in special instances, the electrocardiogram does not permit etiological or pathological diagnosis nor does it measure the functional capacity of the heart Recording the electrocardiogram is an important laboratory procedure but it is only one of the several approaches to the problems *confronting the clinician If the electrocardiogram points* the way to the proper diagnosis the investigation of that particular patient is incomplete until supportive evidence has been disclosed by the other techniques of a complete cardiac examination If the electrocardiogram reveals information which is at variance with the remainder of the clinical studies the situation must be evaluated with exceeding care and the physician must not hesitate to discard an equivocal, unsupported electrocardiographic diagnosis There is a widespread tendency well appreciated by *those familiar with the general level of electrocardiographic* interpretation to give far too much importance to minor changes in the configuration of the electrocardiogram Such errors will be avoided if the electrocardiograph is used always in close conjunction with all the other clinical and laboratory methods available to the physician If these considerations guide the study and use of clinical electrocardiography the method will continue to prove its true worth

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CHAPTER XI (Continued)

PART III

THE PRINCIPLE OF THE REFLEX ARC IN CARDIAC SYMPTOMATOLOGY[1]

By JAMES ORR

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INTRODUCTION

In discussing the symptoms of cardiac disease from the point of view of Sir James Mackenzie's later work it is advisable to state very briefly the reason why this standpoint is regarded as necessary and the general principle on which it is based It will then be possible to consider the relation of this principle to the classification of symptoms generally and of those of heart affection in particular

As disease is only made manifest by the symptoms which it produces it is evident that a clear understanding of the nature of symptoms is of fundamental importance Systematic study of symptoms has hitherto been very imperfectly carried out and the more subtle and elusive signs which characterise the early stages of disease have been almost completely neglected The trend of modern

[1] Sir James Mackenzie suggested the line followed in this chapter and approved of the draft of it submitted to him just before his death (H A C)

investigation has resulted, in the main, in the elucidation of an enormous number of new symptoms and signs of disease, but it has thrown very little light on the way in which these phenomena are produced, how their value is to be assessed and on what basis they are to be classified

In the study of symptoms, it is necessary first to recognise each individual symptom and to differentiate it clearly from others which it resembles second to understand the mechanism of its production, in order to afford a natural basis of classification and third to assess its value in so far as it has a bearing on the future course of the disease Whatever may be the condition from which an individual suffers it is obvious that all the organs of his body are affected in a greater or less degree The disturbed function of one organ reacts on other organs and consequently there is no limit whatever to the number of symptoms which may be discovered The mere accumulation of incidental symptoms of this kind only serves to render an already confused subject more chaotic still

It is fully recognized in all sciences other than medicine that, while the phenomena of nature are exceedingly various in number the laws governing their production are relatively few and there is no valid reason to suppose that symptoms of disease differ in this respect from any other natural phenomena Their manifestations are indeed innumerable but they, like all other natural phenomena must depend for their production on certain well defined laws It was from a recognition of this basic fact that the work of the St Andrews Institute originated for it was realised that, if these laws were discovered a basis of classification would be reached which would make for simplification and enable symptoms to be classed according to their affinity in nature This in its turn would afford a means of identifying the symptoms which are essential for *diagnosis and of differentiating them from those which are essential for prognosis*

We may say then that our starting point is the general principle that while the manifestations of disease are many the laws governing their production are relatively few This is a principle derived from a great general law which is applicable to and demonstrable in relation to every known science The symptoms of disease represent a series of phenomena diverse in their expression but in common with all other natural phenomena manifesting themselves in accordance with certain well defined laws The elucidation of these laws is the object of our study of symptomatology

Taking a broad view of the symptoms of ill health, it will be found that the vast majority of those other than those dependent on mere structural changes owe their origin to alterations of function on the part of certain organs This is demonstrable in relation to any of the symptoms of ill health One need only think of such symptoms as palpitation asthenopia the symptoms of gastrointestinal disturbance, the presence of glycosuria headache, asthma and so on to recognise the truth of this proposition

When such alterations in the functions of organs exist the question at once

arises as to what is the nature of this alteration From the review of a large number of such manifestations one arrives at the generalization that an altera tion in the activity of an organ can only occur and does only occur in one of three ways either by increase of its activity by decrease or suspension of its activity or by the supervention of disorderly activity Increased activity is seen in the symptoms due to contraction of non striped muscle in certain con ditions of rapid heart action etc Decrease or suspension of activity can be recognized in diabetes in so far as the islets of Langerhans are concerned in bradycardias in conditions of skin anesthesia and so on Disorderly activity can be recognized in auricular fibrillation fibrillation of voluntary muscle after section of the nerve and probably also in states of delirium

Having recognized that the majority of symptoms depend upon alterations in the functional activity of organs it is necessary to inquire as to how these alterations in the functions of organs are produced This can only be due to the varying activities of certain processes which normally regulate and control their function In other words all disturbances of the functions of organs including those which give rise to the symptoms of disease are due to disturbance of or interference with certain processes by means of which the activities of the organ are regulated That such a regulating mechanism exists can not be doubted The only alternative would be to regard each organ as an inde pendent microcosm the activities of which varied in a purely fortuitous way without reference to its own needs or the needs of other parts of the body an assumption entirely out of accord with what we know about body activities

If proof were needed of the presence of such regulating mechanism it can easily be found The effect on the function of an organ of section of nerves and of stimulation of the cut ends the modification of these effects by the action of drugs such as atropin the clinical observation of similar effects due to patho logical changes affecting nerve structure the clinical and experimental study of the heart beat the observation of ocular changes in response to drug action and nerve affection all afford indisputable evidence that each and every organ is under the influence of some nervous or other mechanism by means of which its activities are regulated and controlled

A recognition of this fact brings to light an exceedingly important principle viz — that when an organ is disturbed in its function the cause of that dis turbance is not to be looked for in the organ itself or more briefly that all reactions originate in structures other than those which exhibit them As long as the regulating mechanism of an organ is intact and functioning normally the organ must also function normally This of course assumes that the organ is not the seat of any gross structural change

This principle that all reactions originate in structures other than those which exhibit them is of particular interest as it leads directly to that mode of investigation known as the principle of the reflex arc

The Principle of the Reflex Arc

It has been seen that symptoms are produced largely by variations in the function of organs due to agencies affecting the processes by which their activities are regulated The study of this effect in organs is beset with difficulties The organs themselves are of complicated structure, and have elaborate and intricate connections with the nervous system and through it, with each other It is necessary to study these reactions in their simplest expression, which the scheme of the simple reflex may be taken to represent

By a reflex is understood the reception of an impulse by the receptor of an afferent neurone, its transmission to the receptors of an efferent neurone and the production of an effect at the structure with which the peripheral end of the efferent neurone is connected or related If the essential factor in this process be understood the principle can then be extended to explain the functions of organs and their regulating processes which are in themselves merely accumulations of the elements mentioned The significance of this point of view lies in the fact that hitherto investigation has concentrated itself on the end result Certain reactions have been observed to take place in response to various kinds of stimulation mostly stimulations of an artificial kind such as electricity, and no account has been taken of what takes place between the point of stimulation and the production of the end result By this new principle of investigation an attempt is made to arrive at an understanding of the intermediate processes involved

The operation of a reflex arc may be interfered with in any part of its extent between the afferent receptor and the effector organ In each case the result will be the same viz an interference with the function of the organ in question Hence an investigation confined entirely to the effects exhibited in the organs themselves misses altogether the most important part of the process The main object of investigation by the reflex principle is to locate the part of the reflex at which the disturbance takes place Much time might be occupied in discussing questions which the study of the simple reflex process raises It is however sufficient for our present purpose to concentrate on one or two essential points

The first point is that this mechanism only becomes active in response to a stimulus from without The cells of which the body is composed are never entirely at rest They are always either discharging energy or engaged in actively storing it up This is an exceedingly important generalisation when we come to apply the principle of the simple reflex to the function of organs

The second observation of importance for our present purpose is that a cell having discharged its energy is unresponsive to further stimulation until its energy is sufficiently restored This is the law of all or nothing in relation to the individual cell and with it is bound up not only the whole question of stimu

lation of organs but also the problem of their varying activity This may be briefly considered now

Bearing in mind the essential consideration that a cell can only discharge its energy in response to an impulse and that having so discharged its energy it is temporarily unresponsive to further stimulation we are at once faced with two crucial questions namely that of graded stimulation and that of continuous stimulation In other words if cells discharge all their energy how is increased stimulation possible and again if cells are unresponsive once they have discharged their function how is continuous function maintained These two apparent difficulties only represent two aspects of the same question

No organ or functional unit of the body is continually working at its full capacity its cells are not all actively discharging energy at one and the same time This is capable of ocular demonstration in case of the capillaries and can be shown to be true of other organs as well The cells of the organ as it were work in relays increased activity being brought about by a greater number of cells being called into action at a given time Increased stimulation can be brought about in one of two ways either by an increase in the number of functional units involved, or by an increase in the excitability of the cells to which the impulse is conveyed It will be shown later that one of the effects which a regulating structure exercises is that of controlling the rate at which the cells of the organ renew their energy If the impulses follow each other in rapid succession not only does each impulse initiate activity in the receptor cell but also accelerates the rate of renewal of energy in the cell so that its refractory period is shortened and increased activity made possible In the quickening of the heart in response to sympathetic stimulation both agencies can be observed the increased stimulation of the sympathetic itself being due to an increase in the number of neurones involved while the resultant quickening of the heart is due to the increased sympathetic influence raising the excitability of the cells of the sino auricular node facilitating thereby a more rapid discharge of impulses

Again in auricular fibrillation the increased excitability of the auriculo ventricular node is seen in the disproportionate rise in the rate of the pulse in exertion Instead of a rise of from 80 to 90 beats per minute with a normal rhythm a corresponding amount of effort will raise the pulse in fibrillation from 80 to 120–150 per minute This can be controlled in the case of fibrillation by digitalis the rise in rate on effort then approximating that of the normal rhythm This disproportionate increase in rate can only be due to increase in excitability of the cells of the auriculo ventricular node for when digitalis is administered and the rate controlled there is no alteration in the number of impulses which assail the node the only change is in the capacity of the cells of the node to respond to them

The same explanation is applicable to such a condition as that of convulsions e g those following an overdose of strychnine Here there is no increase

in the peripheral stimulation but certain parts of the nervous system have become so excitable that the normal stimuli from the skin, etc, produce the exaggerated reaction seen in the occurrence of convulsions In the case of convulsions as in the case of the heart, clinical observation may demonstrate the presence of both methods of stimulation (increase in the number of neurones involved and increased excitability)

In cases of tetanus we have a condition analogous in its mechanism to the effect produced by strychnine Here again the central nervous system is highly excitable and normal stimuli are sufficient to produce convulsions If the condition improves a stage is reached when the convulsions cease In the early part of this stage the central nervous system is still highly excitable, but not so much so that the ordinary stimuli cause convulsions If, however the skin of such a patient be pinched, convulsions can be induced Here the additional stimulus is obtained by increasing the number of neurones conveying impulses the condition of excitability being approximately constant

The question of continuous stimulation is capable of a similar explanation As only certain of the cells of an organ or functional unit are active at one time the work of the organ is carried out by relays, i e, by alternating periods of rest and activity Failure in the efficiency of an organ occurs when from destructive changes or other reasons the number of cells available for the discharge of its function are diminished in number Hence more and more demand is made on the remaining cells and exhaustion or functional inefficiency supervenes

It remains now to consider the nature of the impulse by means of which these reactions are brought about It must be kept clearly in mind that the *impulse is invariable in its nature It represents a form of energy peculiar to* the living body and found nowhere else When one speaks of a secretory impulse, an inhibitory impulse or a sensory impulse one is not speaking of different varieties of impulses but of different reactions due to the functional peculiarities of the structures which the impulse affects In the case of afferent fibres the peculiar function is situated at the receptor ends in the case of efferent fibres at the effector end This can be demonstrated experimentally by the section and stimulation of afferent and efferent nerves respectively By the same method can be demonstrated the particular part of the regulating process on which drugs act Thus if the vagus nerve to the heart be cut and the peripheral end be stimulated great slowing of the heart results If atropin be administered this reaction does not take place showing that the atropin has acted on the terminal fibrils of the nerve at the sino auricular node Again if large doses of digitalis be administered with the nerve intact slowing of the heart occurs a reaction which is not evident if the vagus nerve be divided indicating clearly that the drug in this instance is acting upon the receptor fibrils at the central end of the nerve

The study of the impulse further brings to light another very important

function of cell activity It has been noted that cells a e never entirely quies cent If they are not actively discharging energy they are actively restoring their energy The result is that impulses are constantly being poured into the nervous system from the skin muscles and other parts of the body As long as the regulating mechanism of the organ is intact the organ will only respond to impulses or stimuli which reach it through the e paths If this mechanism is destroyed say by section of nerve in the case of muscle the mu cle responds to stimuli reaching it from all quarters and exhibits the phenomena of fibrillation This function of control in whatever it consists is es ential for the maintenance of an efficient activity of organs The normal activity of any organ is graded purposive and adapted to the immediate needs of the body When this func tion is lost the organ ceases to show any kind of graded activity but acts ineffec tively and without reference to the needs of the body generally This will be fully illustrated when dealing with the phenomena of loss of control in the regu lating mechanism of the heart itself

The application of this principle of the reflex arc affords an entirely new basis for the classification and investigation of the symptoms of di ease per mitting them to be classified according to their affinity in nature We have seen that in the function of organs two groups of cells are concerned —

(a) Those cells which discharge the particular function of the organ

(b) Those cells which generate and convey the impulses

The latter group of cells form the structures which regulate the functional ac tivity

The symptoms of disease are caused by disturbance of some part of the regulating structure Such di turbances give ri e to one of three results —

(1) An increase in the number of impul es

( ) A decrease in the number of impul es

(3) A cessation of the generation or conduction of the impul es

These results in the regulating processes give rise to three different reactions or symptoms in the related organs namely —

(1) An increased activity of the organ

(2) A decreased activity of the organ

(3) A disorderly activity of the organ or a cessation of activity

The application of this principle in investigation has for its object —

(1) The detection of the part of the reflex arc the disturbance of which is causing the symptoms

(2) The nature of the disturbance

It should be noted further that this process not only affords a basis of classi fication of symptoms but also supplies a key to progno is Hitherto prognosis has been largely a matter of individual experience based on the observation of various cases over long periods of time The recognition however of the rela tion of symptoms to the processes involved in their production eventually will place the problem of prognosis upon a sound scientific basis for it is obvious

that certain of these processes are immediately essential to the maintenance of life, while others are not and the outlook in any given cases of disease must depend entirely upon whether the processes which are involved do, or do not, include those which are necessary for continued existence It is, of course, of paramount importance to be able to recognise the indications to which the involvement of such processes gives rise *As far as the heart is concerned these* will be indicated in discussing the symptoms of heart affection

The Application of the Principle of the Reflex Arc to Cardiac Symptomatology

It is not possible within the limits of a single chapter to do more than give a mere outline of the application of this principle to the heart It will be necessary to limit its consideration to two main points the question of cardiac failure and that of cardiac irregularity To do this intelligibly one must consider first, certain points in connection with the structure of the heart itself

In the heart, as in other organs we recognise two great structural elements, one concerned in carrying out the function of the heart, and one concerned in regulating and controlling its action The former is represented by the musculature of the auricles and ventricles the latter by what is at present known as the conducting system of the heart including the two nodes and the auriculo ventricular bundle The sino auricular node is situated in the auricle near the mouth of the superior vena cava The auriculo ventricular node is also situated in the right auricle, near the opening of the coronary sinus From the auriculo ventricular node the bundle descends into the ventricle dividing into two branches one for the right and one for the left ventricle

Hitherto the bundle has been regarded as a pure conducting mechanism by means of which impulses were conveyed from the node to the ventricle much in the same way as an impulse is carried along a nerve fibril There are however good grounds both experimental and clinical for assuming that this view of the function of the bundle is not altogether accurate Ishihari and Nomuri have shown that the bundle is a cellular structure which in the excised heart can be seen to exhibit active contraction Further, they have shown that the contraction of the bundle takes place at the same rate as the contraction of the ventricle The bundle is thus a structure which is capable of active contraction It is also capable of *initiating the contraction of the ventricle when cut off* from the influence of the auriculo ventricular node as in conditions of complete heart block The bundle is thus not merely a passive conductor but is actively engaged in generating and discharging the impulses which result in the ventricular contraction For this reason it has been found advisable to discard the term "conducting system" altogether and in the remainder of the description it will be referred to as the "genetic system"

The innervation of the heart is maintained by the action of the vagus and the sympathetic nerves These nerves are distributed to the sino-auricular node and the auriculo ventricular node They do not appear to be distributed at all to the bundle for reasons which afterwards will be apparent While there is no evidence clinical or otherwise that the efferent fibres of the sympathetic pass beyond the nodes it is probable that the afferent fibres pass into the auricle and ventricle their existence being implied in the production of cardiac pain

Heart Failure

The study of the principle of the reflex arc in its relation to the heart presents the problem of cardiac failure in an entirely new aspect and explains much that has hitherto been incapable of interpretation principally in that it affords a rational explanation of the process on which the exhaustion of the reserve power of the heart depends

Heart failure depends on the incapacity of the heart muscle to maintain a circulation adequate to the needs of the body In the early stages this inefficiency is only observed when a certain demand is made upon the heart Later the inadequacy is evident even when the body is at rest The indications of inefficiency are usually those either of breathlessness or of pain These symptoms it will be noticed are those which are produced by undue exertion even if the heart is healthy The question of inefficiency of the heart muscle is arrived at by a consideration of the amount of effort which is necessary to produce them that is to say on the degree of prematurity of their occurrence

When the heart is healthy and the body is at rest only a limited number of the muscle fibres are necessary to maintain an adequate circulation When exercise is undertaken impulses are thrown out from the contracting skeletal muscles which are conveyed to the receptor fibrils of the sympathetic nerve and thence to the sino auricular node It has been pointed out previously that stimulation of a nerve consists in the calling into play of an increased number of neurones In addition to this when an impulse acts upon a cell the rate at which that cell restores its energy after discharge of its function is increased Thus when the sympathetic is stimulated by impulses from the body muscles a greater number of its neurones are engaged in conveying impulses to the node more cells of which are affected and the rate of their discharge quickened In this way more muscle fibres of the heart are brought into action to meet the increased demand and the rate of its action is increased

When part of the musculature of the heart is destroyed by degenerative changes or in any other way the number of cells available is reduced and in extreme cases may be exceedingly limited In this case when an extra demand is made upon the heart exhaustion supervenes on account of the fact that the individual cell is being called into action more frequently and its normal period of rest shortened

It will be seen that the "all or nothing" theory of the contraction of the heart, at least, in so far as its action in the living body is concerned, cannot be maintained. Indeed, at the present day, it is not consistently maintained even by those who render it homage academically. Physiologists have been unable to offer any other explanation of such phenomena as the alternating pulse or of the small ineffective beats in fibrillation other than that of the contraction of a limited number of muscle fibres, an explanation which is entirely inconsistent with the "all or nothing" view. As a matter of fact, the "all or nothing" view was based upon the results of electrical stimulation, and is a purely experimental result quite different from anything which occurs in the body itself.

THE MECHANISM OF CARDIAC IRREGULARITIES

By far the most striking phenomena which the heart exhibits are those associated with irregular action. There has always been a tendency to view irregular action of the heart as necessarily of very serious import. While it is true that many types of irregular action are associated with conditions of grave import, the presence of an irregularity by itself is of comparatively little importance. The outlook in any such case depends not upon the irregularity as such, but upon the way in which the heart muscle responds to any embarrassments which the irregularity may impose upon it. It will be shown that, by tracing the irregularity to the process concerned in its production, much light is shed upon the prognostic significance of the various irregularities. As a general proposition it may be stated that all irregularities of the heart owe their origin to a modification in the function of the genetic system. This modification may be produced in any one of the three ways described above, viz., by increase in activity, decrease in activity, or cessation of activity.

Modifications in the Activity of the Sino Auricular Node

The rate of the heart, when the normal rhythm is present, depends entirely upon the activity of the sino auricular node. When the activity of the node is modified all the chambers of the heart participate in the resultant action. Alteration in rate may occur in response to exertion, as a result of drug action or of the toxins. The rate of the heart is entirely a question of the activity of the sino auricular node. It has nothing to do with the efficiency of the muscle.

At the present time certain tests for estimating the efficiency of the heart muscle have been employed based on alterations in rate in response to exertion. By the method, however, of tracing the origin of altered action to the process concerned in its production, it is evident that such tests, if they have any value at all, do nothing more than test the stimulability of the node itself and give no information whatever as to the state of the muscle. It is true that continuous

very rapid action may result in exhaustion of the heart muscle an exhaustion which will manifest itself by the usual signs of breathlessness or of pain The exhaustion however is a result of the rapid action the rapid action is not indicative of exhaustion It is necessary to insist on this as continuous rapid action is frequently regarded as an indication of degenerative changes in the heart muscle Degenerative changes may be associated with rapid action but the rapid action does not depend upon these changes as such for the most extensive myocardial damage may exist without any rise in the pulse rate whatever The presence of a persistently rapid pulse in endocarditis is sometimes quoted as indicating the relation between structural damage of the heart and rapidity of action but this conclusion is not warranted That such rapid action occurs in endocarditis cannot be doubted but it occurs with equal frequency in inflammation of any other organ of the body It is a purely nodal phenomenon presumably due to the action of the toxins of disease upon the node structure and as an index of myocardial efficiency has by itself no more significance in conditions of inflammation affecting the heart than in those affecting any other part of the body

When the number of impulses from the node is decreased a condition of slowing of the whole heart results This has been termed a true bradycardia because all the chambers of the heart participate in the slow action This can be distinguished from a slow action due for example to heart block by the fact that the rate in the former alters in response to exertion

A characteristic form of irregularity known as the youthful type of irregularity occurs in children and young people This type of irregularity is usually associated with respiration and is manifested by a quickening of the heart rate during inspiration and a slowing during expiration If a polygraphic tracing of such a condition be analysed it will be seen that all the chambers of the heart are participating in the irregularity indicating that it depends upon variations in the activity of the sino auricular node Occasionally an irregularity of this type is present which does not seem to be directly related to respiration but in this case also the irregularity is one in which all the chambers of the heart take part

This irregularity being purely nodal in origin has no prognostic significance as far as the efficiency of the heart is concerned

Sup Vol II

Increase in the Activity of the Genetic System

The Extra Systole

In the normally acting heart the cells of the genetic system do not discharge their impulses except in response to impulses received from the sino auricular node It occasionally happens however that the cells of the genetic system become more excitable than those of the sino auricular node and dis

charge their impulse in advance of the nodal impulses This results in a premature contraction, either of the auricle or ventricle according to the particular part of the system where the discharge occurs This form of contraction is known as the extra systole If the premature contraction occurs in the auricle the resulting ventricular contraction is usually full and efficient If it occurs in the ventricle the contraction is usually inefficient and may be imperceptible in the radial pulse

The prognosis in extra systole is based upon the same reasoning as was applicable to the sinus irregularity For a long time the extra systole was supposed to depend upon the heart muscle for its production and was accordingly viewed with some suspicion as indicating possible impairment of the muscle, but as it owes its origin simply to a variation in the regulating system, it has of itself no sinister significance This is in accord with experience for there is no recorded case where an impaired response of the heart could be attributed to the presence of extra systoles In this connection, it is important to note that the extra systole tends to appear when the body is at rest and to disappear when exertion is undertaken, i e, it is present when the heart is working well within its capacity and disappears in the circumstances in which any impairment of the heart muscle would be likely to show itself

Paroxysmal Tachycardia

In all types of extra systole the rhythm is under the dominance of the sino auricular node except where it is broken in upon by premature contraction of the ventricle or of the auricle and ventricle this disturbance being usually limited to a single beat There are conditions however, in which the normal rhythm is not immediately resumed but where the genetic system continues to send out its impulses in advance of those of the sino auricular node for a series of beats which may last for a considerable length of time This constitutes a group of abnormal rhythms to which the term "paroxysmal tachycardia" is applied In the classification of abnormal rhythms adopted here the term is restricted to this particular group because the mechanism of their production differs from that of fibrillation and flutter and also from the forms of increased rate which depend upon excitability of the sino auricular node The characteristic features of such attacks are a sudden increase in the rate of the pulse which lasts for a variable time and which disappears as suddenly as it appeared The suddenness of onset is due to the fact that the excitable part of the genetic system begins throwing out its impulses in advance of those of the sino auricular node and that as soon as it ceases to do so, the sino auricular node at once resumes control, immediately terminating the rapid action

The different forms of this type of tachycardia depend upon the part of the genetic system which is disturbed If the part of that system situated in the auricle is affected, both auricle and ventricle participate in the resulting tachy

cardia If on the other hand the branches of the auriculo ventricular bundle are affected the pulse beats are of the same character as those of the ventricular extra systole the rhythm of the auricle being maintained throughout and independently of ventricular beats Occasionally this form of tachycardia may arise in the auriculo-ventricular node itself the auricle and ventricle in this case contracting simultaneously

In this type of case although the impulses from the genetic system take precedence over those from the sino auricular node the control exercised by the node is not altogether lost In the ventricular type this is evidenced by the regular action of the auricle and in both types by the fact that the node is ready to take complete control immediately the premature impulses cease Further the resulting heart beats are of an entirely different character from those which occur when the influence of the node is entirely lost

Cessation of Activity of the Sino Auricular Node

Auricular Fibrillation

When the influence of the sino auricular node is entirely lost a striking change occurs in the action of the heart The auricle no longer contracts in an orderly and purposeful manner but passes into the condition known as fibrillation

Freed from the control of the node the rhythmic contraction of the auricle ceases entirely Activity of a kind is present but it is a disorderly and ineffective activity of which the rapid and unsystematised contraction of individual muscle cells is the main characteristic a condition precisely similar to that which occurs in skeletal muscle when the nerve control is lost It was a recognition of the important fact of the disappearance of all evidences of auricular activity that led in the first published clinical account of this condition to its being described as paralysis of the auricle

The effect of the loss of control of the sino auricular node is not confined to the auricle but is very definitely manifested also in the auriculo ventricular node

In dealing with stimulation it was noted that the influence of a controlling structure on the cells with which it is related is twofold There is first the initiation of impulse discharge from the cells affected and second a modification of the rate of renewal of energy in the cells It is possible that these two functions are really manifestations of one and the same process From this point of view all that the nerve or regulating process does is to hasten or retard the rate at which the cell restores its energy after discharge of its function the actual discharge of the impulse being determined by a certain flash point in the cell itself

Whether this be so or not there is much in the study of cell activity which

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of ventricular muscle cells which contract in response The portions stimulated eem continually to vary a tendency which becomes greater with increased excitability induced by bodily effort When the rate is slow the diminished excitability of the nodal cells permits them to act more together and a more efficient contraction of the ventricle results When the rate is slow the normal relation of the size of the beat to the length of the preceding pause is sometimes observed

Auricular Flutter

Closely related to fibrillation and probably of similar origin is the condition known as auricular flutter In this condition the auricles contract at a rate of approximately 300 per minute the ventricle sometimes responding to every second beat of the auricle at other times responding to a varying number of impulses producing an irregular pause suggesting that of fibrillation The response of the heart to bodily effort is however widely different in flutter If the pulse is regular in the neighborhood of 150 per minute exercise as a rule has no effect whatever upon the rate If it affects the pulse at all it does so by doubling its rate the ventricle in this case responding to every beat of the auricle instead of to every second beat but this is a very rare occurrence If the pulse falls below 150 it generally becomes irregular It may be regular on account of the ventricle responding to every three four or six impulses but here again any alteration in the rate results in the pulse becoming irregular This effect of exertion on the pulse is a valuable help in the clinical diagnosis of the condition In flutter as in fibrillation the variability in the ventricular rate depends upon the variable response of the cells of the auriculo ventricular node

Decreased Excitability of the Genetic System

When one part of the genetic system ceases to function the initiation of ventricular contraction is taken up by some part of the system below that part which has so ceased It has been seen that in fibrillation ventricular contraction is initiated by the auriculo ventricular node When the bundle is cut off from the impulses from the auriculo ventricular node as in heart block the initiation of the ventricular contraction takes place from the bundle Short of a complete cessation of impulses from the node to the bundle portions of the genetic system are liable to a decreased excitability giving rise to varying degrees of the condition which has been termed heart block This term is not a good one having been devised at a time when the bundle was presumed to conduct impulses in the same way as they are conducted by a nerve and suggests a condition of things which does not really exist It is however retained as being the term in common use and also to avoid adding new terms to an already overloaded terminology

affords support to the view that the regulating mechanism of organs exercises a well defined function of control over the rate of renewal of energy in the cells which come within the sphere of its influence, the behaviour of the auriculo ventricular node in fibrillation being one of the most important Thus, as long as the sino auricular node is active, the auriculo ventricular node responds to impulses conveyed from it and only to those, discharging in its turn impulses to the bundle which result in orderly and effective contractions of the ventricle When the control of the sino auricular node is lost, the effect on the auriculo ventricular node is manifested in three ways (1) the cells of which it is composed show a greatly increased excitability (2) it becomes subject to the action of a shower of impulses from the auricle, and (3) it does not regulate the movements of the ventricle to meet the demands of the body The fact of the increased excitability of the cells of the node and their failure to co-ordinate the contractions of the ventricle with the requirements of the body is seen in the effect of exercise When exercise is undertaken in this condition, the rate of the pulse may rise from 60 to 70 beats per minute to 130 or higher As the impulses from the auricle are approximately constant, one may conclude that this increased rate depends upon increased excitability of the cells of the node itself The effect of digitalis points in the same direction It has been shown already that digitalis acts by stimulating the receptor fibrils of the vagus nerve The effect on the node is shown by a remarkable slowing of the pulse and by the control of its rate when exercise is undertaken This is not associated with any alteration in the activity of the auricle the number of impulses from the auricle remaining as before In this case also a modification of the excitability of the cells of the node is the determining factor

A further effect of the action of the uncontrolled auriculo ventricular node is seen in the nature of the ventricular contraction produced In the normally acting heart the contraction is full and effective Even when the heart is at rest and only comparatively few muscle fibres are being called into action with each contraction the contraction is nevertheless always complete and effective In fibrillation on the other hand the amplitude of the contraction especially when the ventricle is contracting rapidly is variable and ineffective A tracing of the pulse in fibrillation brings to light the important fact that the size of the beats in this condition bears no constant relation to the length of the preceding pause a large beat following a short pause and vice versa In all other irregularities the size of the beat bears a definite relation to the length of the preceding pause This is well seen in the large beat which follows the pause after an extra systole and is due to the fact that the longer pause permits a greater amount of blood to accumulate in the ventricle and also permits of a greater number of muscle fibres participating in the contraction, the latter factor being dependent upon the number of impulses which the auriculo ventricular node discharges In fibrillation there is a wide variability in the rate of recovery of the cells of the auriculo ventricular node resulting in a corresponding variability in the number

brought about by a lesion affecting the bundle itself and preventing the impulses from the node reaching the cells of the bundle below the lesion

When both the sino-auricular node and the auriculo ventricular node are completely out of action there is produced a combination of heart block with auricular fibrillation It will be seen that one of the most important characteristics of the genetic system of the heart is that when any one part of it is put out of action the cells of the part near the ventricle take on the function of initiating the heart beat When the bundle itself fails to function and no impulses are discharged from it to the ventricle the condition of ventricular fibrillation is induced

To sum up a study of the mechanism of the simple reflex arc discloses the all important fact that a cell never functions actively except in response to a stimulus without and that variations which occur in the manifestations which the functional activity of cells affords are due not to any variation in the nature of the impulse but to a variation in the number of impulses received or in a variaion in the capacity of the cell to respond to such impulses such variation being dependent upon the rate at which the cell i capable of renewing its energy

Thus in considering the variations in the movements of the heart we start from the general proposition that the phenomena exhibited by these movements are in themselves dependent upon the reception of impulses from some regulating mechanism The only structure in the heart from which these impulses can come is that consisting of the nodes and their associated structures which we have termed the genetic system By accepting this fundamental proposition and by considering the conditions to which a variation in the number of impulses discharged from the various parts of the system would give rise it is found that all the abnormal rhythms which have been observed in the heart are capable of being classified on a uniform basis and that the individual phenomena observed are similarly capable of a uniform and rational explanation Further this principle of classification is one the application of which is not confined to symptoms exhibited by the heart but is capable of extension to those manifested by the functional variations of every other organ in the body and affords a means by which the innumerable symptoms of ill health may be reduced to a logical order and renders them capable of explanation and of classification on the broad basis of their affinity in nature rather than upon the structural or pathological condition with which they may happen to be associated

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In the very early stages of this condition, a graphic record shows that the inter systolic period, i e, the period which elapses between the contraction of the auricle and that of the ventricle, is lengthened If the sequence of the heart beat be analysed at this stage it will be found that the whole heart is taking part in the contraction in the normal sequence The auricle is contracting regularly, and the contraction of the ventricle is full and efficient, but manifesting a slight irregularity The site of the disturbance in these circumstances can be located in the cells of the auriculo ventricular node The cells of the node do not respond as quickly as usual to the impulse received from the auricle the indication of this being given by the delay in the contraction of the ventricle In a slightly more advanced stage an occasional ventricular beat may drop out altogether If a graphic record be analysed at this stage again it will be found that the auricle is contracting normally At one point however the contraction of the auricle fails to elicit any response in the way of a ventricular contraction Here the excitability of the cells of the node has become so depressed or, in other words the time required for the recovery of their energy has become so increased that at the time the auricular impulse arrived they were not themselves capable of discharging an impulse At a still later stage when the decreased excitability of the nodal cells has progressed still further, it is found that the ventricle only responds to every second beat of the auricle Lastly a condition is arrived at where there is complete dissociation between the action of the auricle and that of the ventricle the auricle contracting in response to the sino-auricular node while the ventricle pursues its course independently of, and quite uninfluenced by the auricular contraction

In *these conditions of heart block* as in all other cardiac conditions, the pulse as representing the contraction of the left ventricle, only indicates the end result or the effect of the disturbed process They too, like the other disturbances of movement in the heart, can be traced back to their source of origin The decreased number of impulses from the genetic system which result in these conditions may be due to various causes The activity of the node may be depressed e g, by the actions of the toxins of disease or it may occur as a sequel of the infections such as influenza diphtheria, etc In these cases the heart block tends to disappear on return to health It may also be brought about by nerve influence In this group of cases the decrease in the activity of the cells of the genetic system is due to the action of the toxin in modifying the rate of recovery of the cells The majority of cases however, would appear to be due to degenerative changes In consequence of these the number of cells available for carrying on the function of the system becomes limited with a corresponding shortening of the periods of rest of the cells which remain and their consequent exhaustion If such a process of degeneration advanced sufficiently far as to render the node totally incapable of functioning the condition of complete heart block would supervene Complete heart block, however, is generally

CHAPTER XII

CONGENITAL MALFORMATIONS OF THE HEART AND LARGE VESSELS

By JOHN THOMSON

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INTRODUCTION

The congenital malformations of the heart form a subject of great interest to the embryologist and the pathologist For the physician in the present state of our knowledge these conditions have far fewer attractions Their physical signs are generally so obscure and equivocal that a confident diagnosis of the lesions present is only occasionally possible during life and even when it can be made it is not very often of any practical value for the prognosis of the case and the treatment of the patient have nearly always to be decided by quite different considerations

The structural defects which may be found in these cases vary extremely both in kind and in degree and their combinations are very numerous It is much commoner to find several lesions present than one only and in some forms of malformations the diagnosis is apt in older patients to be further complicated by the occurrence of secondary endocarditis

The following summary includes all the more important types of malformation of the heart and large vessels and gives an idea of the very great variety of lesions which may be met with In its preparation and in that

is returned to the lungs The septa are always incomplete as otherwise the child could not live The cases that live longest are those in which the ventricles communicate so freely that there is practically only one ventricle The pulmonary artery is usually stenosed Cases of transposition of the large vessels are not very uncommon

(j) *Reversion of the Heart* such as occurs in transposition of the viscera This uncommon condition is frequently accompanied by irregularities in the arrangement of other parts of the heart

(k) *Imperfect Separation of the Aorta and Pulmonary Artery*—Irregularities in the division of the truncus arteriosus are rarely met with They vary in character

(l) *Patent Ductus Arteriosus*—Under ordinary conditions the ductus arteriosus contracts rapidly after birth and is entirely closed somewhere between the tenth and twentieth days of life The two main factors which contribute to this normal process of involution are the physiological lowering of the blood pressure in the pulmonary artery the aorta and the duct itself which occurs at birth and the strong muscularity of the wall of the duct It is therefore frequently found patent in cases in which the blood pressure is kept up after birth by the presence of atelectasis or other lesions of the lungs or by the presence of other cardiac malformations and it is probable that an abnormal lack of muscle or other defect in the wall of the duct may in some instances favor its remaining open The form of the patent duct and the size of its lumen vary greatly in different cases In some it remains cylindrical in some it is funnel shaped with the larger end toward the aorta In a few it presents a spherical aneurysmal dilatation Occasionally cases are met with in which an open ductus is the only lesion present The pulmonary artery may be greatly dilated and the left ventricle is often enlarged

(m) *Malformation of the Semilunar Valves*—Abnormalities in the number and size of the semilunar valves are not uncommon One of the segments may be unusually small or there may be two or four of them instead of three Such conditions are generally of themselves of no importance but it is said that in later life the abnormal valves are especially liable to be affected by endocarditis

2 *Imperfect Formation of Septa*

(A) *Defects in the Interauricular Septa*

(a) *Absence of Septum between Right and Left Auriculoventricular Orifices* the cusps of the two valves being continuous through a widely open interventricular opening The condition is analogous to that which occurs in air breathing fishes The malformation is always accompanied by other

of the section on the diagnosis and prognosis of particular malformations the writer is largely indebted to Professor Arthur Keith's[1] Hunterian Lectures and to Dr M E Abbott's[2] excellent and very comprehensive article on congenital defects of the heart

Summary of Congenital Malformations of the Heart and Large Vessels

1 *Malformations of the Bulbus Cordis*

(a) *Incomplete Fusion of the Infundibulum with the Body of the Right Ventricle* so that there is a constriction left between these parts This malformation is usually complicated by the presence of an interventricular opening a patent ductus arteriosus or foramen ovale or pulmonary stenosis from adhesions of the valves Secondary endocarditis is frequent

(b) *Partial Arrest in the Development of the Infundibulum (Congenital Pulmonary Stenosis)* —This is rarely accompanied by an open ductus arteriosus or a patent foramen ovale

(c) *Complete or Almost Complete Arrest in the Development of the Infundibulum* —In this condition the pulmonary artery is almost or altogether obliterated There is always an interventricular opening and the ductus arteriosus is patent in thirty per cent of the cases The patients are extremely feeble and live only a short time

(d) *Pulmonary Stenosis from Fusion of the Semilunar Valves* —This is usually although not always accompanied by defect of the infundibulum

(e) *Partial or Complete Absence of the Body of the Right Ventricle with More or Less Development of the Infundibulum*

(f) *Subaortic Stenosis* —Due to partial persistence of the bulbus cordis

(g) *Congenital Aortic Stenosis* —Said to be specially rare in Great Britain The first four of these conditions are relatively common and the last three are all very rare

(h) *Coarctation of the Aorta* is not a very uncommon malformation It consists in a narrowing and sometimes in a complete atresia of the descending arch at or immediately below the so called "isthmus" of the aorta which lies between the origin of the left subclavian artery and the ductus arteriosus This portion of the aorta often remains considerably narrower than the rest of the vessel for some months after birth Two forms of the defect are described by Bonnet[3] In the one—the "infantile type —the narrowing is diffuse and in the other—the adult type —it is more or less abrupt In the infantile type severe malformations of the heart are often present but in the adult form of the lesion these are rare

(i) *Transposition of the Arterial Stems* —In complete transposition the venous blood is sent back into the general circulation and the arterial

importance The heart may be displaced to the right side (dextrocardia) or out of the thorax (ectopia cordis)

(a) *Dextrocardia* —In very rare instances the heart may be displaced to the right without any other malformation being present In the great majority of cases however dextrocardia occurs as part of a general trans position of the viscera The general health is usually unaffected

(b) *Ectopia Cordis* —In this condition the organ is displaced either forward so as to lie on the surface of the body upwards into the neck or downwards into the abdominal cavity When the displacement is forward there is either a congenital fissure or an entire absence of the sternum and some of the rib may also be defective In severe cases the pericardium may be absent In most instances ectopia cordis is inconsistent with life for more than a few hours or days

4 *Atrophy of the Left Auricle*

Atrophy of the left auricle with complete obliteration of the mitral orifice is found in rare cases in still born children

5 *Hearts with One Ventricle*

The appearance of a single ventricle may be due either to the presence of an extremely large interventricular opening or to the interventricular septum having become applied in the process of development either to the right or to the left side of the heart

CAUSATION OF CONGENITAL MALFORMATIONS OF THE HEART

The malformation of the heart represent in most cases an arrest of normal growth and development and in a few they depend on an interference with normal processes of atrophy of fetal structures which should have occurred in the organ in utero Many of the patients present a number of obviously developmental defect of other organs such as atresia of the anus hypospadias deformities of the digit or the ears umbilical hernia cleft palate harelip or transposition of viscera and there seems every reason to believe that the causation of all such malformations is essentially similar in nature though unfortunately we know at present very little about their beginnings

Until recent years many of the appearances found in congenitally malformed hearts such as thickening and puckering of valves and adhesion of their cusps were regarded as the result of intrauterine endocarditis but Keith has given strong reasons for believing that this was a mistake and that congenital malformations such as those of the heart are due generally if not always to non inflammatory processes When endocarditis is found in a case of congenital defect of the heart it has therefore probably always been secondary to the fault in development

grave lesions such as transposition of the large vessels or pulmonary stenosis Death usually occurs in childhood

(b) *The Foramen Primum*—This rare malformation consists in a peculiar defect in the interauricular wall It does not necessarily interfere with the normal action of the heart

(c) *Patent Foramen Oval* —The foramen ovale is widely open in the fetus but very little blood passes through it at the time of birth The opening is generally not completely closed until the middle of the first year and quite often a small valvular aperture persists into adult life This scarcely amounts to an abnormality it does no harm and under certain circumstances it may even be an advantage

(d) *Absence of the Septum Ovale*—When the opening in the foramen is large and not valvular or when there is more or less extensive defect in the adjacent interauricular septum it is a real malformation and may give rise to serious disturbance of the circulation Sometimes it is the only defect discoverable but it is much more common to find it along with other malformations of the heart and large vessels

(e) *An Abnormal Foramen in the Posterior Part of the Interauricular Septum* is sometimes met with but is very rare

(f) *Premature Closure of the Foramen Ovale Sometimes Occurs*—Its influence on the occurrence of other malformations is not known

(g) *Abnormal Septa in the Left Auricle* are only found in very rare instances

(h) *Interbulbar or Infundibular Foramina* are occasionally met with in the septal wall of the infundibulum of the right ventricle which communicate with the left ventricle under the right coronary cusp

(B) *Defects in the Interventricular Septum*

(a) *Interventricular Foramen*—The normal interventricular septum closes early in the second month of intrauterine life A persistence of this opening is one of the commonest malformations of the heart The defect is almost always situated at the base and its commonest site is just anterior to the undefended space The opening varies much in size in different cases It occasionally occurs alone but generally it is accompanied by other malformations especially by defects of the pulmonary artery The current of blood through it is usually from left to right

(b) *Irregular Interventricular Foramina* are occasionally found elsewhere in the septum They apparently represent persistent interstices in its original muscular sponge work

3 *Congenital Displacements of the Heart*

Congenital displacements of the heart are rare and of little clinical

death These figures may not however represent sufficiently the proportion of uncyanosed cases for in them the condition of the heart is often overlooked or made light of while those who are deeply cyanosed are pretty sure to find their way to a hospital sooner or later Still found cyanosis present in only thirty four per cent of his cases

The amount of discoloration varies extremely in different cases When well marked it is often darker in tint than that produced by any other pathological condition Generally speaking the prognosis is unfavorable in proportion to the degree of the cyanosis It is often particularly severe in those cases in which the pulmonary artery is much affected When it is extreme it may be accompanied by some puffiness of the features but edema of the extremities is rare and only occurs late in the course of the case In most instances the cyanosis is present at birth and persists through life though it may vary in depth from day to day according to the general health of the patient It may only begin when the child is several years old and it may steadily increase or diminish as time passes In a very few cases it disappears altogether Severe cyanosis never occurs in childhood as a result of ordinary endocarditis and in that disease cyanosis only sets in along with other symptoms of heart failure

Many theories have been formed to explain the cyanosis of congenital malformation of the heart but none of them can be regarded as alone capable of accounting for it The most important etiological factors on which stress has been laid by various writers are three in number (a) admixture of venous and arterial blood through abnormal openings (b) venous stasis and (c) deficient aeration of the blood and two other subsidiary features have also to be taken into consideration (d) dilatation and new formation of peripheral capillaries and (e) the polycythemia and other changes in the blood

It is probable that the causation of the cyanosis is not only a complicated phenomenon but that it varies in different cases and even in different stages of the same case The deficient aëration of the blood which is the main factor is in all probability brought about by various causes including the admixture of venous and arterial blood and venous stasis There can also be no doubt that the great enlargement and new formation of the capillaries in the skin and elsewhere (Carpenter[6]) and the increased darkness of the blood must also contribute to an important extent to the depth of the discoloration

Peculiar attacks of paroxysmal cyanosis are met with not very rarely they occurred to a varying degree in more than ten per cent of my cases Sometimes they set in in children who are habitually cyanosed but often as Variot and Sebilleau[7] have pointed out they occur in children in whom there is no cyanosis at other times They may be accompanied by a

Very little then is known as yet about the conditions under which arrests of development occur, but probably anything that interferes with the health of the mother during early pregnancy may favor their occurrence. One curious and interesting point which may have some bearing on the question is the very large proportion of cases of mongolism that suffer from congenital heart lesion (A. E. Garrod[4]). Some lesion of this kind was present in no fewer than 38 cases out of 250 mongols of different ages of whom I have notes (i.e. 15.2 per cent), and out of 150 of these children who were under three years old the heart was defective in 29 (i.e. 19.3 per cent). The significance of this striking fact is not apparent.

While it is probable that debility of the mother from any cause during early pregnancy predisposes to the occurrence of congenital defect in the heart and other organs, there seems no reason to think that either rheumatism or syphilis in the parents has any special influence in this way. Occasionally two or more cases of congenital cardiac malformation occur in the same family.

Symptoms and Physical Signs

The main phenomena by which we recognize the presence of congenital malformation of the heart may be divided into three groups:

1. Cyanosis, which is usually accompanied by polycythemia and increase of the hemoglobin in the blood, and often also by clubbing of the fingers and toes.
2. Peculiar physical signs discoverable on inspection, palpation, percussion, and auscultation, which are generally very different from those produced by the action of endocarditis on a previously normal heart.
3. Various indications of circulatory disturbance, such as general debility, infantilism, dyspnea, and heart pain, also occasionally recurrent epistaxis and epileptiform seizures of various types.

There are several forms of malformation, however, which may be present without causing any symptoms at all, or in which nothing is noticed but cyanosis, a murmur, or debility. While the symptoms generally make their appearance very early in life, there are some cases in which they begin only about the time of puberty, when the rapid growth of the body is throwing an increased amount of work on the malformed heart.

(a) *Cyanosis. Polycythemia. Clubbing of Fingers*

Cyanosis is so striking a symptom in these cases that the term "morbus coeruleus" was formally used as synonymous with congenital heart disease. This symptom, however, though so characteristic, is present only in a minority of instances. In 136 of my cases there were 73 in which it did not occur at all during the time that they were under observation, while in 63 it was either present from birth or developed to some degree before

death These figures may not however represent sufficiently the proportion of uncyanosed cases for in them the condition of the heart is often overlooked or made light of while those who are deeply cyanosed are pretty sure to find their way to a hospital sooner or later Still[5] found cyanosis present in only thirty four per cent of his cases

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sensation of severe dyspnea and by pain which is evidently extremely distressing and is difficult to relieve Sometimes at least they are occasioned by dyspepsia and they may end in syncope or convulsions or even in death The symptoms of these attacks are described below under heart pain'

Polycythemia —In cases with cyanosis the red blood corpuscles are usually though not always greatly increased in number Often they amount to from six to nine million in the cubic millimeter, and sometimes even to twelve million This change is believed to be of the nature of a compensatory hypertrophy It is usually progressive and its presence to a high degree is probably always an unfavorable sign The amount of hemoglobin is usually also proportionately increased but the number of the leucocytes is often not abnormal

Clubbing of the Fingers and Toes occurs in most but not in all cases with severe cyanosis It is sometimes present at birth but often only develops after months or years Occasionally it is present in cases in which there is no discoloration When severe it is a bad element in the prognosis As D B Lees[8] pointed out it is less likely to occur when the foramen ovale has remained widely open because under these circumstances there is less tendency to congestion of the systemic venous system When the fingers and toes are much clubbed there is often a corresponding condition of the nose and ears

Clubbing never occurs to a severe degree in young children from acquired heart disease Its presence is therefore a strong point in favor of the lesion being congenital in origin

(b) *Thrills and Murmurs*

The physical signs characteristic of congenital malformations of the heart are many and various On inspection visible pulsation in unusual areas is frequently observed and on palpation alterations in the position and force of the apex beat and coarse thrills are often felt especially at the base of the heart and over the position of the right ventricle In many cases changes in the size and contour of the heart can be made out by palpation and percussion On auscultation alteration in the loudness of the sounds and various murmurs with unusual areas of audition and propagation are commonly met with

The combinations of these phenomena have often much more significance than their individual occurrence Thus a loud systolic murmur with no increased dullness and no accentuation of the pulmonary second sound has a very different meaning from that of an otherwise identical murmur accompanied by the usual signs of cardiac hypertrophy

The murmurs are usually peculiar in their areas of audition and in their lines of propagation which frequently do not correspond with tho e

characteristic of any simple valvular lesion It is often difficult if not impossible to determine the area of their maximum intensity and this may also vary from time to time in the same case In the very great majority of instances the murmurs are systolic in time rarely however they may be diastolic or presystolic Peculiar humming sounds are sometimes met with especially over the base of the heart It is to be remembered that murmurs due to congenital cardiac defects may change considerably in character and their areas of distribution may increase greatly if the patient becomes anemic If the child is dying in a state of great debility the murmurs may diminish very much

(c) *Various Indications of Circulatory Disturbance*

Indications of circulatory disturbamce of various kinds are frequent A severe degree of debility is often found in cases with cyanosis and also sometimes in those in which this symptom is not present and infantilism is not uncommon in many forms of malformation as the children grow older (Carre[9] Jesson[10]) *Dyspnea* is frequently present on exertion although it is absent at other times it is usually absent in cases which are not cyanosed Distressing spontaneous breathlessness generally occurs during attacks of paroxysmal angina

These recurrent attacks of *heart pain with cyanosis* are as has already been mentioned not at all uncommon They usually begin gradually but often become so severe that the child seems quite stupefied and ceases for the time to pay attention to his surroundings Sometimes he seems to lose consciousness altogether or has a convulsion and he may die in the attack Occasionally in infant in whom the murmurs and cyanosis are not well marked attention is first drawn to the condition of the heart by the occurrence of seizures of this kind

Some children with congenital heart disea e in whom the usual symp toms are not very distinct are brought to the hospital on account of recur rent epistaxis or convulsive attacks

Diagnosis of Congenital Heart Lesions

In examining children with obscure murmurs and other signs which may indicate the presence of malformation of the heart the two most important questions to be decided are *first* is the lesion congenital or acquired which is not usually very difficult to determine and *second* if the lesion is congenital how far is it likely to interfere with the heart in the efficient performance of its functions From the point of view of prog nosis and treatment this is the matter of most importance

There is seldom any great difficulty in distinguishing the lesions of acquired heart disease in early childhood from those of congenital lesions Acute endocarditis is rare in infancy and when due as it generally is at

this age to the action of pneumococci or other pyogenic organisms it is usually secondary to empyema or to acute epiphysitis so that the diagnosis is easy

The murmurs which are most frequently mistaken for those of congenital heart lesions are the functional systolic bruits of obscure origin which not rarely occur in the space between the left border of the sternum and the left mammary line and a similar functional murmur over the base of the heart In these cases prolonged observation may sometimes be necessary before deciding the diagnosis Such murmurs are never accompanied by cyanosis or clubbing or by changes in the contour of the heart and they are only rarely either loud or harsh In older children the diagnosis may be further complicated by the possibility of secondary endocarditis having occurred in the malformed heart

The following axioms may often be found useful They are mostly taken from Hochsinger's[11] interesting writings

1 Loud harsh musical murmurs with a normal or but slightly increased area of dullness do not occur in little children except in congenital cases When acquired inflammatory heart affections with loud murmurs are met with at this age they invariably cause great increase in the cardiac dullness

2 The occurrence of murmurs along with greatly increased cardiac dullness and feeble apex beat in young children is in favor of congenital lesions The increased dullness depends mainly on enlargement of the right heart while the left is but slightly altered On the other hand acquired heart disease in children is accompanied by increased force of the apex beat because its effect falls first on the left side while the dilatation of the right heart sets in later and does not affect the strength of the apex beat

3 The complete absence of murmurs at the apex while they are distinctly present in the region of the auricles and over the pulmonary orifice is always an important element in the differential diagnosis and is more in favor of septal defects or pulmonary malformations than of endocarditis

4 Abnormal weakness or absence of the pulmonary second sound along with a distinct systolic murmur can only be explained in early childhood by assuming the presence of congenital pulmonary stenosis

5 Absence of a palpable thrill in spite of very loud murmurs audible all over the precordial region occurs almost exclusively in cases of congenital septal defects and is therefore against a diagnosis of acquired heart disease

6 Loud systolic murmurs (especially those accompanied by a thrill) which have their point of maximum intensity over the upper third of the sternum and are unaccompanied by any indication of marked hypertrophy of the left ventricle are very important for the diagnosis of

persistence of the ductus arteriosus and cannot be explained by the assumption of endocarditis of the aortic valves

7 A murmur in the second left interspace a short distance from the sternum which begins after the first sound lasts through the second sound into the long pause and is accompanied by a corre ponding thrill and accentuation of the pulmonary second sound is usually caused by a patent ductus arteriosus (Gibson[1]) *In some cases however the systolic murmur produced by this lesion* is shorter and ends before the second sound

8 The presence of congenital defects in other parts of the body is in favor of any heart affection which is present being of congenital origin

General Prognosis

In those cases of congenital heart disease which are examined in early infancy little help can usually be got in the prognosis from the murmurs present This has to depend in most instances on the child s general strength *the character of the pulse the pre ence or absence of cyanosis and on en*largement of the heart and liver Generally speaking it is unfavorable in proportion to the degree of cyanosis and clubbing of the fingers which is present but in some serious cases the cyanosis is usually slight though paroxysmal attacks of it may occur from time to time Many of the cases die within the first few weeks of life and probably two thirds of them before the end of the second year If the baby is well grown well nouri hed and vigorous however with little or no cyanosis and no increase of the cardiac dullness an unfavorable prog-o is as to his future should not be lightly given until he has been some time under observation The loudness of the murmur has no influence on the prognosis

In older children the same data have to be taken into consideration In most of the less severe ca es however the chief and only satisfactory way of estimating the patient s fitness to grow up and enjoy life like other children and of judging how much or how little he should be allowed to do is to inquire into the functional capacity of the heart To do this we must find out what exertions he has been in the habit of making without suffering from any signs of dyspnea or undue fatigue and we may also test the response of the heart to effort by trying how much he can now do without discomfort

*A tendency to bronchial catarrh has an unfavorable effect on the prog*nosis as in these children even slight bronchitis is apt to end in bronchopneumonia For this reason also measles and whooping cough are particularly dangerous to them Their liability to ulcerative endocarditis has al o to be taken into consideration

When a child with congenital heart di ease i suffering severely from

general debility it is always important before giving a serious prognosis to make sure that the symptoms complained of are due to the state of the heart and not to other causes I have several times seen children who had a congenital cardiac malformation and were supposed to be dying from it but whose alarming symptoms were really the result of other causes altogether such as infantile scurvy severe rickets or some other food disorders and who rapidly recovered strength under suitable dieting

Diagnosis and Prognosis of Particular Lesions

Stenosis and Atresia of the Pulmonary Tract

Pulmonary stenosis is probably the malformation of the heart most commonly met with in practice According to Peacock[13] more than four fifths of the children with congenital heart lesions who reach the age of twelve are suffering from it It is usually accompanied by patency of the interventricular and interauricular openings one or both and often by an open ductus arteriosus and the presence of these conditions may not only complicate the physical signs but also have an important effect on the prognosis

The clinical phenomena are usually characteristic There is always severe cyanosis and it is especially intense in cases of complete atresia and in those of stenosis in which the septa are intact Generally there is a loud harsh rasping systolic murmur heard all over the precordia with the point of maximum intensity in the second left space transmitted towards the left clavicle and not well heard in the interscapular space behind In some cases however there may be no murmur at all A thrill over the second and third left spaces "is also frequently present when the interventricular septum is entire and also when a defect of that septum co exists with a widely patent foramen ovale when the interauricular septum is closed and the interventricular open a thrill is rare and when it does occur may perhaps be ascribed to the associated septal defect" (Abbott[2]) The pulmonary second sound is often weak or absent but it may be occasionally normal or even increased in loudness

In typical cases a fairly confident diagnosis often may be possible from the localization of the murmur and thrill the increase of the cardiac dullness to the right and the severe cyanosis with absence of accentuation or loss of the plumonary second sound In many cases however the symptons are equivocal

The probable duration of life depends on the degree of stenosis and the state of the septa One of Peacock s cases lived for forty five years but most die in childhood even when the interventricular foramen is patent When the septa are closed or when atresia or extreme stenosis of the vessel exists the child is always extremely feeble and dies within a few months of

birth Acute secondary endocarditis is not uncommon in pulmonary stenosis and many of the patients die of pulmonary tuberculosis

Stenosis and Atresia of the Aorta

Subaortic Stenosis is a rare condition and generally gives rise to no symptoms until well on in adult life The constricted part is then very liable to secondary endocarditis and it is this which usually produces the symptoms which are similar to those in acquired aortic stenosis

Congenital Stenosis and Atresia of the Aortic Orifice is extremely rare in this country For this reason and because the patients only live for a few weeks or months it has little clinical interest

Coarctation of the Aorta

The infantile type of this deformity is found mainly in babies who die very early and is often associated in them with severe malformations of the heart so that its clinical interest is usually not great A few cases have however been reported in which this condition was found in older children complicated by the formation of a large aneurysm (Brouson and Sutherland[14])

The adult type is met with in older children and adults and in many instances though not in all the patients develop interesting and characteristic clinical phenomena owing to the gradual formation of an extensive collateral circulation through the superficial arteries of the neck and upper half of the trunk

The symptoms include a number of subjective phenomena such as violent headaches sleeplessness and buzzing in the ears along with suffusion of the head and neck and sometimes epistaxis and hemoptysis In other cases there are severe thoracic epigastric and abdominal pains and long standing vomiting and there may also be pains in the back and lower limbs Cyanosis is very rare except as a terminal symptom The signs of a collateral circulation may be present from the first but usually they are late in developing and in some cases they do not appear at all Many of the patients in whom they occur are strong able bodied men in whom the circulation has been recently overtaxed or endocarditis has supervened The subclavian and carotid arteries enlarge and pulsate and the internal mammary posterior intercostal scapular and other smaller vessels also become increased in size and tortuou The left side of the heart may enlarge The sounds may either be pure or accompanied by loud murmurs

When these characteristic signs appear the diagnosis may be easy When they are not present the condition may not be recognizable The progressive development of the symptoms and physical signs is an

important point in the diagnosis Even when the characteristic symptoms occur however it is not always easy to distinguish them from those due to pressure on the aorta by an intrathoracic tumor or to an aneurysm In some latent cases the malformation has little or no effect on the dura tion of life In others death occurs from rupture of the heart or aorta and in some from heart failure

Transposition of the Arterial Stems

At birth the child is well grown and well developed as the malforma tion does not cause any disturbance of the fetal circulation Cyanosis may be present from the first but usually it does not set in till after some days or weeks This may be connected with the closure of the ductus *arteriosus (Thérémin*[15]*) When the pulmonary artery is not stenosed* the cyanosis is not severe and it may be absent Clubbing may or may not be present A systolic murmur is often to be heard but as there is usually a patent ductus arteriosus or a septal defect it may be due to one or other of these conditions Often no murmur is present and according to Hoch singer the presence of extreme cyanosis with pure heart sounds and ac centuation of the pulmonary second sound at the base of the heart gives sufficient grounds for a diagnosis of this condition in an uncomplicated form

The prognosis is unfavorable for though a few patients have survived *to adult life, the great majority of them die within the first year* The cases which live longest are those in which the ventricles communicate so freely that there is practically only one ventricle

Patent Ductus Arteriosus

When this lesion is uncomplicated by other cardiac malformations there is usually no cyanosis until late in the progress of the case and the patient often lives many years in the enjoyment of good health and without any abnormal subjective sensations Cardiac hypertrophy and other signs of embarrassment of the circulation may however supervene sooner or later in some cases and recurrent dyspneic attacks with epistaxis hemopty sis or hematemesis are not very uncommon In the end the patient may die from heart failure

Physical signs are almost always present There may or may not be increase of the cardiac dullness A thrill usually systolic in time and con tinuous through the whole cardiac cycle is fairly often felt The murmurs vary in character they are nearly always systolic in time A very prolonged murmur which is specially characteristic of the lesion has already been described

In rare instances an infant who presents signs which seem *to* indicate the presence of an open ductus gradually loses them all and grows up with a perfectly normal heart (Thomson[16])

Patent Foramen Ovale

The symptomatology of this condition is obscure and during life its recognition is practically never possible When it occurs alone it may give rise to neither symptoms nor physical signs but cyanosis is sometimes present and murmurs of various kinds are often met with for which no other causes can be found These are not only diastolic and presystolic as might have been expected but very frequently systolic in time The area of their maximum intensity also varies in different cases but they have generally been loudest over the third and fourth left costal cartilages In rare instances in which a patient with this defect acquires mitral incompetence in later life the defective state of his interauricular septum may be betrayed by the occurrence of a very marked venous pulsation in the neck without any evidence of tricuspid disease

The prognosis in cases in which there is a large defect in the interauricular septum is obscure Many of these cases die in early infancy but not a few instances are on record of individuals with a severe degree of this lesion who have reached adult life and some even old age It must however be remembered that the presence of a free opening between the auricles will constitute a danger to life should anything of the nature of venous thrombosis occur A detached fragment of a thrombus carried to the right side of the heart is apt to pass directly into the left auricle and thence through the left ventricle into the arterial system causing embolism in the brain or elsewhere

Defects in the Interventricular Septum

A persistent opening in the interventricular septum may give rise to no symptom or physical signs but in about half the cases in which it is the only lesion more or less cyanosis is present In a smaller proportion —about a third— a systolic thrill is felt which may be confined to the base or felt all over the precordia A harsh murmur over the third and fourth left spaces well heard in the interscapular region behind is present in most instances even when the opening in the septum is very small It is usually systolic in time but it may be diastolic The character of the murmur may vary considerably in different cases A positive diagnosis of the defect is not possible

The prognosis is on the whole less favorable than in cases of patent foramen ovale It causes more interference with the circulation and leads to cardiac hypertrophy at an earlier stage Cases have however been recorded in which patients with this lesion have lived from forty to forty five years The danger of the occurrence of embolism is the same as in cases of patent foramen ovale

Treatment

Most children with congenital heart lesions require to be treated continuously as invalids and a good deal may be done to prolong their lives and promote their comfort and happiness if their habits are so regulated as to prevent unnecessary exertion excitement all causes of chill and indigestion, which are apt to aggravate their symptoms They should always have a period of rest in the middle of the day and their slightest ailments must be carefully treated on their first appearance School life is generally out of the question for them When anginal attacks occur carminatives should be given after meals and inhalation of amyl nitrite tried If this fails to relieve their distress as often happens some form of opiate is indicated In the cases in which there are signs of heart failure epistaxis and convulsions digitalis is sometimes useful but it has no effect on the cyanosis and other symptoms in most cases of congenital heart affection

There are not a few children with loud murmurs from congenital heart disease who have no abnormal fatigue or discomfort on exertion and who require no special treatment, as they are practically in good health These should certainly be allowed to run about freely and exert themselves reasonably in other ways as much as they like Anesthetics and surgical operations are no more dangerous to them than to other children

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CHAPTER XIII

CHRONIC DISEASES OF THE HEART

By SIR JAMES MACKENZIE

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INTRODUCTION

We are still so ignorant of the factors underlying the causation of heart disease that it is impossible for a writer to describe the subject of this article in that simple and comprehensive manner which a full and complete knowledge of the subject would permit A lack of knowledge of the cause of phenomena in nature compels a description of the manifestations as if they were distinct entities This leads to a great accumulation of detail and renders a subject like disease of the heart confused and difficult of comprehension If an earnest endeavor be made to understand the nature of the phenomena which disease produces certain principles are revealed which admit of such an arrangement of the subject as enables the knowledge limited though it be to be used intelligently in the practice of medicine

The origin and the insidious progress of heart disease are in the majority of cases hidden from us and we are only brought face to face with heart disease after it has gone beyond the hope of cure let alone prevention The circumstance that brings a heart affection to light is generally some experience of the patient some sensation of distress which compels him to seek the doctor s advice When the doctor examines the patient he often

finds the mischief already done and all he can do is to guide the patient's future life in paths that will conserve the heart's strength Fortunately the detection of the trouble is often so early that by giving sensible instruction we are able to render valuable aid not only in prolonging the patient's life but in many instances in enabling the patient to lead a useful life and one free from suffering

The means by which this can be done demand a thorough knowledge of the signs which the heart in health and disease can exhibit The heart is an organ which gives excellent opportunity for its study It is however played upon by so many influences that a knowledge is required of its behavior under a great variety of circumstances There is in many respects a resemblance between the manifestations evoked by a healthy heart under certain influences and those evoked by hearts affected by disease so that it is necessary to have a clear conception of the nature of the symptoms otherwise confusion arises and the practice of medicine is rendered haphazard and uncertain

As disease or impairment of the heart is revealed by symptoms in order to gain a means of estimating the significance of symptoms an orderly arrangement of symptoms based upon some clear principle is necessary To that end I give at the outset a classification of symptoms which not only is based on sound physiological principles but gives the doctor who grasps the meaning of this classification a guide in practice and research

In the present state of knowledge of heart affections it is impossible to give a complete picture of the diseases but it is possible to describe essential matters which will be of the greatest value in recognizing the significance of the symptoms which we may detect This is done by having a clear conception of the nature of the problem *viz* the possibility of heart failure The question in every case which confronts the doctor is, is this heart failing or do these signs indicate the presence of heart failure or do they foreshadow its occurrence?

The question of heart failure is therefore of the first importance and before a doctor can with assurance treat or give an opinion as to the patient's condition he must have a knowledge of what signs are evidence of heart failure After dealing with the classification of symptoms I shall discuss this question of heart failure The conclusions drawn from the discussion reveal a simple method by which the heart's efficiency or the degree of heart failure can be estimated Indeed the method is so simple that many people do not realize that it is based on sound principles and so dissatisfied with it seek after more tortuous and recondite methods I therefore, deal at length with the steps that were taken to bring to light the manner of perceiving heart failure as described here so that the reader may appreciate not only how heart failure may be discovered but also

the methods which clinical medicine requires for the solution of such problems

As the manner in which the subject is dealt with is somewhat different from that usually pursued inasmuch as it deals mainly with the detection of symptoms and the estimation of their significance in place of a description of the morbid conditions producing them—a description which lack of knowledge prevents my giving—I would respectfully request the reader to grasp fully the meaning of the first three subdivisions of this chapter (classification of symptoms heart failure normal and abnormal signs) as I have found that the knowledge which they contain tends greatly to simplify the practice of medicine and affords a knowledge on which a reasonable prognosis and therapy can be based

Classification of Symptoms

When we make an examination of an organ we are on the outlook for physical signs We have been taught that in health the heart has a certain position in the body a certain shape that its rate and rhythm have certain characteristics and that the sound have certain peculiarities Any departure from what has been recognized as normal is considered a physical sign of disease produced by some structural change so that we have a group of *structural symptoms*

In an organ like the heart the question of its functional efficiency arises and this is shown by the manner in which it maintains the circulation The signs of an inefficient circulation are not shown by the heart but by the manner in which the circulation is maintained in other organs and there arises a series of symptoms indicative of heart failure due to functional inefficiency so we get a group of *functional symptoms*

When the heart muscle is not supplied with sufficient blood or is itself the seat of disease or impairment its forced activity gives rise to a set of symptoms the outcome of muscle exhaustion symptoms of suffering and distress as pain calling for a cessation of effort These symptoms arise through a mechanism which involves the nervous system so that there are produced certain symptoms nervous in origin and protective in function thus we get a group of *reflex symptoms*

Symptoms then can be classified into three groups structural functional and reflex In addition there are secondary symptoms As repeated references will be made to these groups a short description is given here of their peculiar nature and significance

Structural Symptoms—It is necessary to hold clearly in mind what is revealed when we detect a physical sign either by the unaided senses or by means of the many mechanical devices employed in their detection

In the main a physical sign implies an alteration in the structure of an organ though this class includes also such signs as the modification of the sounds and movements of the heart The detection of a physical sign gives little information beyond the fact that a change has taken place in the organ There may arise from experience a knowledge that certain signs are associated with conditions of a definite nature bearing upon the health of the patient as that an enlarged heart is often associated with heart failure but heart failure is not revealed by a cardiac physical sign It might seem to be a needless refinement to insist upon such a distinction but for the purpose of keeping clearly in mind the limitations of knowledge revealed by a physical sign such a distinction is necessary, for we find that in practice the detection of a physical sign is often thought to convey information far beyond what it actually reveals Thus for the last hundred years the detection of a murmur in the examination of the heart has led to the assumption that the heart was seriously affected and today this view misleads the profession Moreover all the phenomena revealed by mechanical aids (by X rays by polygraphic and electrocardiographic records) belong to this group as well as blood pressure findings

The limited knowledge and the peculiar kind of knowledge revealed by a physical sign always must be kept in view as the neglect of this has misled the profession in estimating the significance of symptoms in prognosis and treatment

Functional Symptoms—The essential matter in the maintenance of health is the functional efficiency of the organs of the body A structural modification may take place and leave the efficiency unimpaired Thus it arises that after the detection of any physical sign a careful inquiry must be made into the efficiency of the heart

Functional symptoms are rarely detected from direct evidence in the heart but rather from the effects produced on other organs While the heart s condition and activity can be so easily studied the information essential to a knowledge of its efficiency can only be made out by the reaction on other organs As I have said the study of the heart s various manifestations gives no idea of its functional efficiency and this knowledge can only be acquired by observing how the circulation is maintained in other organs as shown by dropsy or enlarged liver due to heart failure Even in the slighter degrees of heart weakness the essential signs are brought about by a failure of the heart to supply sufficient blood to parts remote from the heart as the center for respiration The nature and significance of functional symptoms will be demonstrated in dealing with heart failure

Reflex Symptoms—There are a great many diseases in which we fail to detect any structural sign or any functional impairment yet we can recognize the disease with great accuracy The signs by which we are able to

do this result from the irritation of a limited portion of the central nervous system by a peculiar form of stimulation produced by the diseased organ Thus in certain forms of appendicitis the only signs may be a sense of uneasiness or pain in the right iliac region an excessive sensitiveness to pinching and pressure of the skin and deeper structures of the abdominal wall and a rigidity of a portion of the muscle wall in this region There also may be present a frequency of micturition All these phenomena may speedily disappear after the removal of an inflamed appendix In affections of the heart we may get a similar class of symptoms as pain situated across the chest and in the arms hyperalgesia of the skin and muscles in these regions

When we group all these symptoms together we are driven to seek for a solution through the nervous system Such symptoms as a hyperalgesia of the skin with a contraction of the muscles indicate the involvement of sensory and motor nerves supplied to the external body wall and the stimulus producing them can only arise from some place where their nerve centers lie close together with the nerves from the heart Such a center is found in the central nervous system

In heart affections the nerves supplying the skin and muscles of the affected region have their cells of origin in the section of the spinal cord from which arise the seventh cervical and first second third and fourth dorsal nerves From this region the sympathetic nerves supplying the heart arise Therefore we can say that the symptoms present in such a case are due to an irritability of the spinal cord—*an irritable focus of the spinal cord* we find a group of symptoms produced by a reflex stimulation of the central nervous system which affords a valuable aid in the recognition of the patient s complaint and which will be described further on

Secondary Symptoms —Not only may the physical signs and symptoms of impaired functional efficiency and the reflex phenomena be manifested by diseases of the heart but the heart may show symptoms as a reaction to the modified function of other organs Probably the depraved function of every organ reacts upon the heart either through the nervous mechanism of the heart or from its nutrition being impaired Infections may play upon the heart either from the direct effect of the microbes or from their toxins

The recognition of a class of symptoms which are secondary and due to the functional disturbances of other organs or to infection is necessary because it gives a line of investigation in each case Already we know of many symptoms produced by different organs which are associated in their appearance and we recognize certain groups of symptoms as due to the altered or impaired function of an organ so that the appearance of one of a group leads to a search for others

This matter is of importance from the standpoint of treatment It is manifest if the heart is disturbed by the depraved functions of other organs how useless any treatment will be which is devoted to the heart Yet this view needs emphasizing for to my knowledge large numbers of individuals are submitted to prolonged treatment for cardiac symptoms in which that organ is only secondarily affected Indeed so important is this aspect of the matter that the question should arise in every case whether the symptoms are not provoked by some other organ or by some general disease in which the cardiac manifestations are but a part

THE SIGNIFICANCE OF SYMPTOMS

The importance of the classification of symptoms just given will be realized by demonstrating its practical application When a patient consults a doctor it is because he is not feeling well A doctor in his examination of the patient in addition to hearing the patient's account of his trouble may detect some physical sign There is a tendency to associate the sensations of ill health with the presence of the abnormal sign This is apt to occur with an abnormal cardiac sign for in practice we find many people who have been warned of some obscure danger because their doctors had detected a murmur or an irregular action of the heart or an increase in the blood pressure Many of these warnings are quite unnecessary and have arisen because there exists a great defect in medical knowledge This defect consists in a lack of knowledge of the significance of symptoms

When a doctor detects an abnormal sign in his patient the mere detection of the sign is but a preliminary step in his examination There is much more required of him The patient expects that he will be able to tell how that sign came to be there and to foretell what will happen if the cause producing the sign is left untreated The doctor is also expected to know if the cause is amenable to treatment and what is the appropriate treatment

This kind of knowledge commonly included in the term prognosis has not received that attention which it deserves The need for this knowledge meets the practicing doctor in the examination of every patient and is so essential to him in his work that it might have been supposed it would have called for a thorough investigation Strange as it may seem no subject in medicine of equal importance has been studied so imperfectly and inefficiently It is tacitly assumed that it is a subject easy of understanding and needing no particular training for its pursuit Nothing could be further from the truth for it is a subject that requires for its pursuit a very profound knowledge of the manifestations of disease It can truly be said that its importance has never been fully recognized nor has it been realized how essential it is to the intelligent practice of medicine So little

has the subject been appreciated that it has not even been understood how a knowledge of the subject can be acquired

The basis for a knowledge of this kind requires a recognition of all the manifestations of disease so that they can be clearly differentiated the one from the other not only in regard to the mechanism of production but as to the bearing the cause of each symptom has on the patient's future To accomplish this all the usual methods of clinical examination are necessary, but carried out with a clearness of purpose that has been wanting in a great measure It is manifest that the significance of an abnormal sign can only be found by watching individuals who manifest it during the period of life when it is present As the abnormal sign may be present for long periods of years the observer must have the opportunity of being in contact with the affected individual for a long time The vast majority of signs can only be assessed properly when consideration is given to the presence or absence of associated phenomena therefore in addition to watching individuals who present an abnormal sign it is necessary that the observer should be on the outlook for other signs The nature of these other signs and the manner of searching for them will be understood if the significance of the classification just given be fully grasped On the detection of a structural or physical sign the functional efficiency of the heart must be inquired into The recognition of this necessity will direct attention to the kind of evidence required to complete the examination of the patient The manner in which the knowledge for assessing the value of cardiac signs can be acquired will be shown under the next heading

Heart Failure

The impaired health that results from a weakness of the heart and the danger to life that frequently occurs in disease of the heart have surrounded all questions associated with the heart with an atmosphere of dread The medical profession are ever inventing new ways for studying cardiac disturbances The result of this study has been to employ numerous methods for the detection of signs that might give warning of impending danger As the source of danger has been imperfectly realized new methods *are being continually invented in the hope that new* light might be thrown upon the matter but on account of the lack of understanding of the manner in which heart failure is brought about such investigations are haphazard and result in the employment of methods unsuited for the purpose and in the accumulation of details that obscure the issue It is necessary to have a clear idea of what heart failure is and how it is brought about and for that purpose I deal here with the subject in some detail in order to show that the principles underlying the production of heart failure are of simple kind

and that when they are understood the recognition of heart affections becomes comparatively easy while treatment is rendered rational and effective

The Importance of the Heart Muscle in Maintaining an Effective Circulation —The purpose of the circulation is the supply of a constant stream of material capable of nourishing the tissues and the removal of such waste products as are capable of entering the circulatory channels As a continuous pressure is required to force the blood onwards the intermittent pressure conveyed to the blood stream by the heart is converted by the resiliency of the arterial walls into a constant pressure at the periphery of the arterial system The maintenance of the arterial pressure is the outcome of the force exerted by the ventricles and of the resistance of the smaller arteries and capillaries The full force of the ventricular contraction is not spent on the blood current merely during the period of systole In throwing the blood into the arterial system ventricular contraction does so with such force that it distends to a slight extent the larger arteries The elastic coats of the arteries as soon as the ventricular systole is over compress the column of blood within them and in this manner maintain a degree of arterial pressure during the period that the ventricle is not acting The ventricular force is thus stored up by the distension of the elastic coats of the arteries and liberated during ventricular diastole

The heart muscle supplies the force which maintains the circulation while the various parts of the mechanism of the circulation are so adjusted that all parts combine to facilitate the work of the heart and to attain the object of the circulation A disturbance of that adjustment interferes with this mechanism and throws more work upon the heart muscle So long as the heart can overcome the impediment and maintain the circulation in a normal manner no symptoms are evoked but if the heart muscle is embarrassed and is no longer able to carry on the circulation efficiently then certain phenomena arise at once and these phenomena we call symptoms of heart failure

From this consideration it will be realized that *heart failure is simply an inability of the heart muscle to maintain an efficient circulation* and that this failure of the heart muscle is due to the muscle having some impediment embarrassing it in its work or to some defect in the muscle itself This failure may arise from exhaustion when the circulatory organs are healthy or from a disturbance of the normal adjustment of the various factors concerned in the circulation This disturbance in fact may arise in a great many ways but the final result is the same that is to say embarrassment of the heart muscle and its final exhaustion

The Rest and Reserve Forces of the Heart Muscle —In order that the essential signs of heart failure may be recognized and the mechanism of

their production understood a study of the heart both with the body at rest and during effort gives the means for acquiring this necessary knowledge As the heart possesses the power not only of maintaining an efficient circulation when the body is at rest but of varying its activity according to the bodily requirements the force inherent in the heart muscle may be considered for practical purposes to be composed of two parts that is to say a part which is employed to maintain an efficient circulation when the body is at rest and which therefore may be called the rest force and a part which is called into action when effort is made and which may be termed the reserve force The rest force is the minimal force which the heart has to exert to maintain the circulation at a level consistent with life The impairment of this rest force produces those evidences of heart failure which persist when the body is at rest such a dropsy and dyspnea The continuance of such impairment eventually leads to a fatal issue

The second part of the heart s force (reserve force) is that which is called upon when the body makes some effort While the body is at rest this potential force is not exercised but its possession enables us to undertake with ease all forms of effort Inasmuch as this part of the heart s force is only used when exertion is made it may appropriately be called the reserve force of the heart

The Beginning of Heart Failure—Heart failure is shown first by a limitation of the reserve force An individual becomes conscious of this limitation by finding that some form of exertion which he was used to perform with ease now causes distress Heart failure invariably starts in the first instance by exhaustion of the reserve force The exhaustion is slight at first but by the persistence of the causal factors it proceeds apace until after a period long or short this exhaustion induces such distress as to compel attention or the rest force is encroached upon and with the exhaustion of the rest force a point of danger to the life of the individual is reached

When a healthy individual undertakes some form of severe bodily exertion—for example running at the top of his speed —there comes a time sooner or later when he suffers a temporary exhaustion of his reserve force Ultimately on account of this temporary exhaustion he is compelled to desist If he attempts to run again before he has a period of rest sufficient for the restoration of the muscle he will not be able to maintain his full speed during so long a period as in the first instance If he systematically denies himself a sufficient period of rest his powers of endurance will gradually become more and more restricted This which we recognize as natural in a healthy individual is identical with the process occurring in an individual having some cardiac defect whether the defect is due to disease of the heart itself or to other factors which embarrass the heart in its work

It will be seen therefore that exhaustion of the reserve force in individuals with enfeebled hearts is of the same nature as exhaustion of the healthy heart and that heart failure in the first instance is simply the premature exhaustion of the reserve force of the heart No doubt exhaustion in diseased hearts can be brought about in a greater variety of ways than exhaustion in healthy hearts but this consideration is not germane to the point at issue Whether it is an affection of the heart muscle which tends to induce the exhaustion or the irregular action of the different parts of the heart or the too great frequency of the rate of contraction or a valvular lesion the result is always the same and the laws governing the production of the symptoms are the same The only difference between a man in fair health and a man with an affection of the heart which limits his efforts is that in the case of the latter certain disagreeable sensations are provoked more readily than in the case of the former The sensations are identical in kind Any modifications they may show in different states of health are quantitative only The patient with a heart affection no doubt tends to suffer a greater degree of exhaustion than the man possessed of a healthy heart but the mechanism by which the sensations are produced is identical

It is evident that if the rest force is intact the individual when at rest will present no signs of heart failure It is also evident that in the early stages of heart failure the signs of exhaustion will only be found when an effort has been made as it is only then that the limitations can appear That there is a limitation can be known in the very early stages only to the individual affected In other words the evidence of heart failure in the early stages is entirely subjective the individual becomes conscious of certain sensations of distress or discomfort on making an effort which before this time he was able to make without experiencing these sensations As the heart failure advances these sensations are provoked by less effort, until finally the rest force becomes encroached upon then we get objective evidences such as dropsy and labored breathing while at rest

Conditions That Induce Heart Failure —I have already remarked that in the normal condition the adjustment of all parts concerned in carrying on the circulation is essential to efficiency and that any disturbance of the adjustment at once calls for an increased effort on the part of the heart muscle Such calls are made first on the reserve force and if persisted in lead sooner or later to its exhaustion The causes are extraordinarily varied in character and may arise from a disturbance of any of the factors on which the normal circulation depends It is from this standpoint that diseases of the heart should be considered inasmuch as it is only by looking at the matter in this light that a proper perspective is obtained in regard to the significance of any abnormality Thus irregular action of the heart should be described from the point of view of its effect upon the efficient performance of the

heart as well as the condition producing it. Valvular defects should be studied not as specific affections to be considered in themselves but rather as a source of embarrassment to the heart muscle in its work or as indicating the presence of a lesion that may have extended to the muscular wall. In the same manner arterial degeneration and high blood pressure should be considered as conditions which upset the normal adjustment of the factors which carry on the circulation. Inherent defects of the muscular wall itself should be viewed in relation to their bearing on the heart's efficiency.

To appreciate the meaning of heart failure we must, as has been indicated, bear in mind that the force maintaining the circulation is the heart muscle. There is a limit to the amount of work which a healthy heart muscle can perform. It is the forcing of the heart to work beyond this limit that produces heart failure. We are justified, therefore, in looking upon heart failure as the expression of an exhausted heart muscle.

It will be clear from the foregoing that the sensations produced by exhaustion of the heart muscle, however easily provoked they may be, give no clue to the underlying morbid condition. This fact must be borne in mind. The actual morbid condition present must be determined by the consideration of other evidence revealed by the history and by the physical examination. The sensations, however much they may vary in degree, are common to all forms of heart impairment. The well known fact that certain sensations are apt to occur more readily with some affections than with others, as for example pain in aortic disease, in no sense alters this fundamental truth.

The Functional Efficiency of the Heart

On account of its accessibility to examination and the ease with which its activities can be studied, the heart is a very suitable organ for the purpose of studying its functional efficiency. In a manner this has been done from time immemorial, for the taking of the pulse has that object in view. But though the importance of the subject may have been realized, and many attempts made, both by clinicians and physiologists, to find out, like much else in medicine, it was not understood how the inquiry should be pursued. Attempts have been made to acquire the knowledge by experiments on animals, and the introduction of every new instrument during the last hundred years, from the introduction of the stethoscope to the latest laboratory contrivance, has arisen from an attempt to solve the problem.

The failure of these attempts was due to the fact that the only way this object could be achieved was not understood. The recognition of impaired efficiency can be attained only by using those methods that are peculiar to clinical medicine, *i.e.*, the careful differentiation of symptoms with an

appreciation of their significance and the watching of individual cases with varying degrees of impairment for a sufficient length of time. Hitherto attempts to find out the functional efficiency of the heart have depended mainly on the study of physical signs, as by carefully noting the character of the sounds of the heart and the various murmurs, and how they were affected by effort; by the counting of the heart beats or taking the blood pressure before and after effort; or by means of registering the movements of the heart by sphygmograph, polygraph and electrocardiograph. As these methods discover only symptoms belonging to the structural group of the classification of symptoms, they do not reveal the symptoms essential to the understanding of the functional efficiency of the heart.

Symptoms Which Reveal the Functional Inefficiency of the Heart

As I have already pointed out, in all hearts there is a reserve of strength only called upon by effort, and the first sign of the heart's strength being impaired is shown by a premature exhaustion of this reserve force. Attempts to acquire a knowledge of this limitation from mechanical devices or laboratory methods have failed. If, however, we study the sensations produced by effort when pushed to the point of exhaustion on all sorts and conditions of people, we observe that there speedily are produced certain phenomena which give the desired information.

At first sight the sensations produced by a failing heart seem so indefinite that no clear conception of their nature or mode of production can be acquired. However, a persistent attempt should be made to have each sensation clearly differentiated. Distressful sensations arise when effort is made beyond a certain limit in people with healthy hearts as well as in people with damaged hearts. In people with healthy hearts the distressful sensation is one of breathlessness as a rule, though in a few people there is a sense of constriction across the chest which almost amounts to pain. When from any cause gradual heart failure sets in, the symptoms are the same but produced by a slighter effort. This is best seen in people getting on in years in whom nothing can be detected amiss with the heart, and the only evidence of impairment is a limitation of the field of response to effort.

While breathlessness, occurring after an amount of exertion that the individual was wont to undertake with comfort, is the most common sign, in some tightness and oppression across the chest are the chief signs provoked, accompanied in some people by pain which in a few become so severe as to present the symptoms which are recognized as angina pectoris.

These two kinds of sensation are those which give the truest estimate of the heart's efficiency. The one, breathlessness, belongs to the functional group of symptoms and arises from the heart failing to supply the center of

respiration in the brain with sufficient blood The other pain and oppression in the chest from the reflex stimulation of motor and sensory nerve centers in the spinal cord provoked by exhaustion of the heart muscle belongs to the reflex group of symptoms This distinction between the signs of functional inefficiency (breathlessness) and of a pure cardiac reflex (pain and oppression) is based on the study of certain peculiar morbid conditions

Breathlessness —When breathlessness arises from cardiac inefficiency it is always found to be associated with a diminished output of blood or rather an output insufficient to supply the respiratory center Physical effort under normal circumstances calls for an increased supply of blood to the active parts This is met by an increase in rate of the heart beat and a dilatation of the vessels supplying the active parts It is unnecessary to dwell upon the fact that there is a limit even in health to the response of the heart to effort that limit being shown by the distress in breathing

This sign of cardiac inefficiency can be demonstrated by the story of certain morbid states to be due to the deficient supply of blood In most cases of auricular fibrillation the response to effort is accompanied by such an increase of rate that many of the beats are so ineffective that little or no blood may reach the periphery and breathlessness is the most clamant symptom in the majority of these cases

As an increased output from the heart is required to supply the active muscles during exertion to meet this demand the heart s rate has to increase In certain diseases the ventricular rate does not increase in response to effort and as a result breathlessness is induced with other signs due to a lack of blood supply In complete heart block the rate of the ventricular beat is steadily about thirty per minute and it does not increase in response to effort When individuals with such an affection hurry in their walk or attempt to run most of them are pulled up by breathlessness A few may feel other sensations as a swaying feeling as if they would fall or their feet feel heavy as if loaded These sensations manifestly are due to a deficient supply of blood to the brain and feet Another instance where the heart s rate is uninfluenced by effort is in auricular flutter Here the auricles usually beat about 300 per minute and the ventricles respond in many cases *only to every second beat the ventricular rate being about 150* Effort has no effect as a rule on either auricular or ventricular rate but it provokes the sensation of breathlessness and not of pain

From these observations it is seen if in response to effort the output of the heart is diminished or not increased breathlessness is readily induced

Pain —The reason for stating pain as an expression of exhaustion of the heart muscle arises from the consideration already given of the reflex group in the classification of symptoms In the study of cases of angina pectoris

it was frequently found post mortem that the coronary arteries were so extensively diseased that for many years the heart could not have received a sufficient supply of blood to enable it to function efficiently Moreover, a consideration of what happens to any muscle when forced to work with an insufficient supply of blood affords confirmatory evidence Thus in cases with degeneration of the arteries of the leg leading ultimately to gangrene the patients for a long time may be unable to walk more than a few hundred yards because they are pulled up by pain in the legs and feet In a patient in whom the femoral artery had been blocked effort beyond a limited extent resulted in pain in the legs of such an agonizing kind that he was compelled to stop In many people in whom the heart is not affected with actual disease but the muscle is weakened from other causes which have impaired the health as toxic affections elsewhere anemia or impaired nutrition with overwork pain is a frequent symptom Accompanying the pain particularly in this latter type there is often hyperalgesia of the skin of the left chest especially under the breast

The pain and hyperalgesia are always present in the field of peripheral distribution of the sensory nerves whose centers are associated in the spinal cord with the centers of the cardiac sympathetic nerves This field of distribution is shown in Fig 3 page 425 Sometimes the pain is felt along the jaw or in the neck in the peripheral distribution of sensory nerves associated in their origin with that of the vagus These people when effort is made are frequently pulled up by the pain and when sufficient rest is not obtained the tendency to pain becomes much increased while the area of cutaneous hyperalgesia enlarges

The Sense of Exhaustion —In the systematic inquiry into the nature of the sensations produced by effort other sensations were recognized the most frequent being a sense of exhaustion or fatigue Although not a cardiac sensation it is so intimately connected with the circulatory system that it needs to be considered This sensation causes a great desire to sit or lie down In many cases it speedily passes off when this can be done If forced to carry on some people become faint and lose consciousness

There are many varieties of this sensation produced in different ways besides effort as in standing in a hot room It is assumed in many cases to be cardiac in origin but it seems to be due to some vasomotor disturbance inducing a cerebral anemia the result of a dilatation of the peripheral vessels with accumulation of blood in them such as in the large abdominal vein or the vessels of the skin especially when the body is rendered warm by exertion and heavy clothing As many of the people who suffer from this are debilitated from other affections the heart is often weak from the same causes but the sensation is not as I have said properly speaking a cardiac one This matter will be more fully discussed later on

Estimation of the Amount of Reserve Force

I have endeavored to find some standard by which the amount of reserve force and its exhaustion could be expressed in terms of precision I have however failed to find any definite standard and when one reflects it will be realized that it is not possible that a measure of such definite precision as to be applicable to all cases should be attainable Since the ability to undertake effort is due to the possession of a reserve force we recognize that in healthy people the amount of reserve force is subject to great variations Among trained athletes there are some capable of much greater endurance than others and the terms short winded and long winded imply really different amounts of reserve force The term training" used in athletics implies amongst other things the aquisition of an increased amount of reserve force This is due to the power possessed by the heart of increasing the efficiency of its functions by their systematic and judicious exercise Conversely the neglect to exercise the reserve force leads to a diminution of its amount as witnessed in the speedy exhaustion of healthy people who lead sedentary lives This latter fact is of importance when the amount of reserve force is limited in people who may present some abnormal cardiac condition In such people the limitation of the field of cardiac response may be due to the lack of exercise of the reserve force

The standard therefore by which we can estimate the amount of the reserve force is in the main personal each individual unconsciously acquiring the knowledge of what he can do So long as he exercises the heart within the limits of his powers no symptoms arise but as soon as the reserve force is exhausted and the effort is persisted in distress and discomfort are experienced Thus it will be seen that the evidence of exhaustion is common to sound and impaired hearts varying only in the ease with which it is provoked The chief requisite in estimating the degree of inefficiency of the heart is thus an experienced physician with a knowledge of the significance of symptoms

Onset of Heart Failure with Patients in Bed

Patients who are confined to bed from illnesses other than the heart may develop heart failure as old people who have to lie in bed because of a broken leg or others who suffer from an exhausting illness as typhoid fever or a pregnant woman Naturally in these no test can be applied nor does reference to their past experiences give much help

If we watch carefully we may find certain early signs which will put us on the alert A slight increase in pulse rate and a slight increase in the rate of breathing should always arouse suspicion The increased rate in breathing may not be noticed unless looked for it is *generally quiet and shallow* and when counted it will be found over twenty per minute An examination will

reveal in many such cases crepitations at the base of the lungs In these cases the examination should begin by asking the patient on which side he lies then make him sit up and auscultate the base of that lung on the side on which he had lain and at the same time ask the patient to take in one full and deep inspiration This opens up the alveoli at the base and if there is any abnormal moisture it is manifested by numerous fine crepitations Healthy people show no sign of this Slightly weakened hearts may show it with the first deep inspiration only if there is distinct cardiac enfeeblement the crepitations do not disappear I have seen cases where the first sign was the crepitation during the first deep inspiration and gradually the crepitation became more persistent until the resonance of the bases of the lung became impaired even to complete dullness with no breath sounds and at the post mortem examination the lungs at the bases have been sodden and airless In some instances there have been patches of inflammation (catarrhal pneumonia—the hypostatic pneumonia of the feeble) I have also seen this hypostatic congestion disappear and as the patient improved the crepitations gradually disappeared the last sign being the crepitations with the first deep inspiration

I have found this method of observation of the greatest practical use In the elderly it governs the position which the patient should occupy—lying down or propped up In typhoid fever it is a prognostic sign of the very greatest value—the absence of edema of the lungs indicating that the heart has escaped while its presence and gradual increase is a sign of great gravity In heart disease it is likewise one indication of the heart s condition and in the complication of pregnancy and heart disease it is one of the most important guides in the management of these cases

It is of no less importance in treatment as will be realized when the reason for its appearance is appreciated It invariably accompanies dilatation of the right heart and the manner of its production seems to be as follows The factors that move the blood through the lungs are twofold first and most important the right ventricle and second respiration In healthy hearts the first of these is so powerful that the second is scarcely appreciated When however the right ventricle is enfeebled the assistance of the respiratory movements becomes necessary When the patient lies in bed on one side the pressure of the ribs on the mattress restrains their movements so that the flow of blood through this part of the lung is retarded and edema results This can be shown in the early stages for when the patient breathes deeply the whole of the crepitations may disappear

Summary

By following a line of observation in which the physical signs and the sensations evoked in response to effort were carefully noted in individual

leading strenuous lives many showing a progressive weakness of the heart all phases of heart failure with the accompanying phenomena were observed and in many who died by obtaining a post mortem examination and having the heart examined by skilled pathologists certain deductions were drawn of a simple kind which became of the greatest service when applied in practice Briefly these were

The heart s efficiency can be perceived by recognizing the manner in which it responds to effort

The first sign of heart failure is shown by a sensation of distress in the individual undertaking some effort he was accustomed to perform in comfort The amount of effort undertaken without distress gives the measure of the heart s functional efficiency

The chief sensations of distress produced by the exhaustion of the heart are breathlessness or a sense of constriction across the chest or pain

These propositions have reference to individuals able to be up and about The signs of heart failure occurring in individuals when confined to bed have been described Extreme forms of heart failure will be described in discussing affections of the myocardium

The Nature of Cardiac Symptoms

Normal and Abnormal Signs —Most organs of the body present certain evidences by which we recognize their presence and experience shows that these evidences are fairly constant and reliable so that certain signs are recognized as normal Departure from normal characteristics is looked upon as possibly indicating the presence of disease though it is well recognized that most organs may show certain modifications which are unusual but nevertheless quite consistent with health Perhaps no organ can show so many variations in its manifestations in health and disease as the heart Not only are the normal variations bewildering in their number but these are so like the manifestations of disease that the utmost confusion prevails as to the meaning of many very obvious signs It is necessary therefore to consider the variations that are consistent with health and to find some means by which the significance of doubtful symptoms may be determined

To a certain extent this has been shown by the steps which were taken to assess the functional efficiency of the heart But this wants a little more elaboration as the signs which in one person may be quite normal in another person may be signs indicating a certain degree of heart failure

Normal Limitations of the Heart s Response to Effort

I pointed out that the first sign of heart failure was a limitation of the individual s power to respond to effort as shown by the appearance of certain

distressful sensations There are a great many healthy people who are normally short winded and who are never able to run far or walk up a hill rapidly without being pulled up by distressful sensations This limitation is quite normal to them though in another individual such a limitation would indicate serious trouble To recognize the difference it is necessary to find out the amount of effort the individual was able to perform at such time as he considered himself to be in fair health and it will be found that in the normal individual there was always present this limitation while in the impaired individual the limitation had come on and progressed in a definite manner from the time when he was able to take such effort in comfort

Normal Variation in Heart Rate—There are great varieties in rate amongst healthy people In children up to ten years of age the rate in the healthy may vary from 120 to 80 and even less In the young adult the variation may be from 100 to between 50 and 60 In adults the variation may be from about 90 to 50 or even a little under The slowest normal acting heart in a healthy man that I have seen was a little under 30 beats per minute With this one exception every case I have observed with a rate under 40 suffered from heart block the result of disease or from an excessive use of digitalis

Normal hearts respond to effort or fever by an increase in rate Damaged hearts also as a rule respond by a much greater increase in rate than normal hearts but the variations are so great that little reliance can be placed upon any degree of increase as a sign of heart efficiency Even in healthy men in good training the rate may become very great after effort reaching sometimes to 200 beats per minute Even the time taken for a heart s rate to fall after cessation of effort is so variable in health as well as in disease that no useful criterion can be obtained from this kind of observation

Normal Variation in Size and Shape of the Heart—The size and shape of the heart may also show considerable variation within normal limits In children the heart is higher up in the chest than in adults so that the apex beat is not infrequently found in the fourth interspace half an inch or even an inch outside the nipple line This high position may be due to the greater relative size of the liver raising the diaphragm or it may be due to the fact that the relation of the heart to the chest wall alters as time goes on The variation of the position and shape of the heart revealed by percussion and the X ray is due to the different shapes of the chest and the varying height of the diaphragm One finds in some healthy people the apex beat in the sixth interspace and in others in the fourth In the female the heart is slightly smaller than in the male

Normal Variations in the Sounds of the Heart—When we consider the factors concerned in the production of the sounds of the heart the taut

stretching of the membranes held in position by bands partly muscular and partly tendinous, the contraction of the muscle of the heart, the variation in the amount of the muscle, the varying contents in the cardiac cavities *and other incalculable factors, we need not be surprised when in practice we find a great variety in the modifications of the sounds of the heart in* people enjoying robust health. The deductions to be drawn from murmurs will be described in the chapter on murmurs; here I merely wish it to be recognized that there are no grounds for supporting the view that the efficiency of the heart can be inferred from any peculiar character of the sounds. When some modified sound is associated with heart failure, there will always be other more reliable signs, while to base an opinion on a modified heart sound is sure to lead the observer astray.

Variations in the Heart with Age.—There is another matter which should always be kept in mind in dealing with the cardiac phenomena, and that is the influence of age, or rather of the changes brought about by the different periods of life. Some of these will be referred to in dealing with special phenomena, such as irregular action of the heart and murmurs, but it is well to recognize that the modifications of the heart's action may produce signs undoubtedly pathological, but of such slight significance that one may consider them as normal to the period of life in which they appear. We all recognize in the face certain lines and wrinkles which we look upon as signs of advancing years, but do not consider them pathological. The graying of the hair, the thinning of the skin, are evidences of advancing years. Such changes which are evident in the external parts of the body have associated with them changes of a similar nature going on in the internal organs. These are most evident in the heart, so that from infancy to old age, in the healthy and vigorous as well as in the frail, changes occur which may be of little moment, but which give rise to symptoms which may easily mislead the unwary. It is incumbent then, when the doctor discovers any sign which he takes to be abnormal, to ask first whether the sign may not be, after all, a physiological manifestation, *or be the outcome of some slight change in* the heart which is due to the changes associated with advancing years, and therefore is of little importance.

These changes, signs of advancing years, are most of them due to a deficient supply of blood to some particular tissue. Thus the thinning of the skin, which makes such a difference between the thick skin of the child and the tissue paper like skin of the old, is mainly or entirely due to a difference in the number of capillaries. In the heart the fine texture of the valves is normally supplied with only a small quantity of blood, and with advancing years the supply diminishes with a consequent thickening and retraction of the fine edges of the valves. The consequence of this is a modification of the sound of the heart, producing muffled sounds and murmurs. These changes

seldom reach a degree which embarrasses the heart muscle in its work and though the noise which they make may seem alarming in its loudness yet they are free from danger Similar changes in other parts of the heart may produce equally innocent signs such as irregularities chiefly of the extra systole kind and occasionally slight changes in the auriculo ventricular bundle producing a slight degree of heart block

The limitation of the heart s power to respond to effort occurring in advancing years has a variety of significance and the rate at which it advances and the extent it has reached have to be carefully weighed in a common sense manner to find out whether it is only such as one would expect at the period of life the patient has reached or whether it is proceeding at such a rate as to raise the suspicion that some disease process is present more active than the senile changes would account for

Variations in the Female Heart—In women during menstruation pregnancy and the puerperium and lactation there are changes more or less marked which should always be reckoned with in estimating the significance of any cardiac sign The most common changes are alterations in the sounds Systolic murmurs come and go in a somewhat bewildering fashion during pregnancy and the puerperium The heart is said to be increased in size during pregnancy but this is far from being settled The increase of the uterine tumor presses up the diaphragm and induces a displacement of the heart so that the apex beat may be found in the fourth space and well outside the nipple line Such a displacement may modify the sounds so that systolic murmurs may be produced But it is difficult to say how they are produced and it would not be profitable to discuss them as we are so ignorant of the factors concerned in their production and my purpose in referring to them here is to insist that no grave significance should be attached to symptoms developed or detected at those times without due consideration being given to the possibility of their being but incidental changes of no significance

With the onset of the menopause it is well known that many phenomena mostly of a nervous character appear In many women at this time cardio vascular symptoms are frequent They are mostly of a vasomotor kind flushing exhaustion and irritability of the heart being the most common Attacks of cardiac pain sometimes of great severity and resembling in some respects those due to serious disease of the heart are not uncommon With these I deal in the chapter on angina pectoris as well as with the areas of hyperalgesia in the left chest, which are apt to appear in women at this period of their lives

Response of the Heart in Affections of Other Organs

Further it must be borne in mind that the heart is extremely sensitive to stimulation from outside sources It is possible that derangement in the function of every organ in the body stimulates the heart either reflexly or from the effect of the deranged function acting directly on the heart or its nervous mechanism This should lead to the scrutiny of the whole individual in every case where the heart is suspected Even where there are well marked signs of disease the examination should not be completed until the possibilities of the heart s state being aggravated from extrinsic causes can be excluded This is particularly the case in febrile attacks as the heart responds to the febrile state in a great variety of ways Each microbe which produces a rise of temperature at the same time manufactures some toxin peculiar to itself and this toxin often reacts on the heart It is for this reason that in some individuals at one time the rate with a slight rise of temperature may be greatly increased while in another febrile attack the temperature may be much higher and the rate of the heart beat much slower

It should also be remembered that during a febrile attack the poison may induce varying degrees of dilatation of the heart and systolic murmurs frequently arise during a simple febrile illness The neglect of this may lead to the suspicion that the symptoms are due to the invasion of the heart itself by the disease and it is not always possible to be certain whether the changes in the heart are due to a temporary poisoning or to the disease affecting the heart The possibilities being recognized the search for associated phenomena will help to settle the matter

The Examination of the Patient

The Patient s Appearance—In every instance when a doctor sees a patient he should rapidly but searchingly scrutinize the patient s face and note the manner in which he walks or the position he assumes in bed If he is in bed the fact that he lies flat or has to have his head or parts of his body raised gives information as to how the heart maintains the circulation when he is at rest On entering the doctor s presence the state of the patient s breathing should be noted as well as his manner whether calm and collected or betraying signs of nervousness and anxiety The fact that a patient may consult the doctor under the impression that he has something wrong with his heart may throw him into a state of excitability that will react on the heart and later on in the examination an increased rate of the heart may be referred to this cause and not taken as an evidence of cardiac trouble

Pallor.—The color of the face gives much helpful information in many obscure cases. The healthy countenance needs no description, as it is one of those matters one knows and recognizes and words fail to convey an adequate description of it. There is a tinge and a color which even in the bedridden at once puts out of count a number of conditions which might otherwise have to be considered. On the other hand, the color of the face often gives a clue to the nature of the condition, as in the anemias, and in cases where a subtle change occurs which may be, and often is, overlooked. As the anemia which is the cause of the pallor often induces cardiac disturbances, many people are supposed to have a heart affection because of these disturbances. While the different anemias may be described in terms corresponding with the results of a microscopic examination of the blood, a helpful appreciation of the condition can be acquired by the physician from the appearance of the patient's face. The pallor of the chlorotic and of the weakly produced by unhealthy surroundings or prolonged ill health should be recognized and distinguished. When the physician sees these signs he is at once given a cue that he will probably have to seek for some other cause of the patient's complaint than the heart. In the serious anemias, as pernicious anemia, the early stages of malignant disease, or the late stages of a microbic infection, the chief complaint may be breathlessness on exertion and palpitation, and the physician easily may be misled because he at the same time detects some abnormality in the heart. This is more likely to happen to the doctor who sees the patient frequently, as the progress of the disease is so insidious that he fails to note the gradual changes which are taking place in the color of the patient's face. Another doctor seeing the patient for the first time may have his attention arrested by the pallor. The pallor in these cases, as a rule, is different from that of chlorosis or the pallor of poor health, in that there is often a faint sallow tinge and the face is a little drawn, a faint alteration in the expression difficult to describe. When any adult, in whom there is no reason to suspect either chlorosis or pallor from poor health or bad environment, shows such an alteration in color, the suspicion should always be aroused that there is some serious mischief present. I have repeatedly observed, particularly in elderly people, that a faint but definite change of this kind heralded the onset of a serious disease.

While the heart in these cases is only affected secondarily, a progressive pallor, it should be remembered, is an accompaniment of a steadily advancing and insidious form of malignant endocarditis. The pallor of empty capillaries, as after an attack of unconsciousness due to standstill of the ventricle as in heart block (Adams-Stokes syndrome), is sometimes very intense. A persistent pallor, sometimes with a dirty color—the earthy countenance—is characteristic of certain cases of aortic regurgitation.

Cyanosis.—In many cases of advanced heart failure the blood is not suf

ficiently oxygenated and the color of the cheeks and lips becomes altered, shading from a slight darkening of the red cheeks and lips to marked blueness. Although it is assumed that cyanosis is a sign of ineffective circulation through the lungs with diminished respiratory exchange, yet there is something else in the matter. Patients with manifestly diminished pulmonary circulation, even with failing hearts, may show no signs of cyanosis, while others show marked cyanosis in whom there is no reason to assume that the pulmonary circulation is interfered with, and when there is no reason to suspect any communication between the right and left sides of the heart permitting an admixture of venous and arterial blood.

Although cyanosis is associated with a great variety of conditions which hinder the oxygenation of the blood from mechanical causes, and is sometimes due to poisoning from coal tar derivatives and certain toxic conditions of microbic origin, there are some in whom the cyanosis is undoubtedly cardiac in origin, and it is then typical of certain diseased states of the heart. One of the most striking is the florid cheeks of a dark red, an appearance which is usually associated with a certain degree of wasting which occurs in a somewhat advanced stage of auricular fibrillation, particularly when associated with mitral stenosis. The appearance of the face is almost diagnostic. It is often associated with a slightly jaundiced tinge, and in these cases the liver will be found enlarged. Some people have a high color, a ruddy face but with a somewhat darker tinge, which many superficial observers would take to be indicative of robust health. I saw recently a young man of twenty five who was passed as fit for the army because of his full blooded looks. It was only when he called attention to a swelling on the backs of his hands and his legs that doubt arose. A careful examination revealed that he suffered from a fairly advanced stage of adhesive mediastinitis of tuberculous origin.

The cyanosis of congenital heart disease (morbus ceruleus) with clubbed fingers is well recognized, but how it is brought about I do not know, for it occurs in cases where there is no deficient septum between the right and left chambers of the heart. A considerable degree of cyanosis of the extremities is not usually cardiac in origin, and it may occur in healthy people, especially in lanky youths on a cold day. This is vasomotor in origin. Its presence in people with heart affections may mislead. I have seen an elderly man who had frequent attacks of auricular fibrillation whose nose and lips became very blue when at rest. Exertion on going up and down one flight of stairs immediately dispersed the blueness.

The Interrogation of the Patient

Realizing the importance of the patient's sensations, great care should be taken to get a good knowledge of their experiences. The questions must be

framed so that the patient recognizes what it is we ask and it is therefore incumbent upon us to have a clear conception in our own minds of the kind of information we are seeking Each question therefore must have a definite object and must be put so clearly that the patient comprehends our meaning we must also insist upon the answer being limited to the question and we must not pass away from the subject until we have got as full an answer as the patient is capable of giving This implies on our part a knowledge of the kind of information the patient is capable of yielding and much training on our part is necessary for us to attain the skill of a competent examiner

The first question bearing upon his condition should naturally be to ask of what he complains The reply to this question should be limited to the *sensations which immediately caused him to consult a doctor* Thus if it is a heart trouble he must clearly specify the sensations he himself experiences as pain breathlessness or exhaustion At first a note should be made of all the sensations of distress or discomfort of which he complains then each sensation should be taken up by itself Thus if pain is complained of the situation in which the pain first appeared should be found out getting the patient to indicate this by placing his hand over the region then the part to which it radiates and the character of the pain as to its intensity and duration whether continuous or intermittent The circumstances provoking the pain as whether it is brought on by effort mental excitement or when the body is at rest and its relation to food should be ascertained With these facts clearly appreciated the first time the pain even in its mildest form was felt and the occasion of its appearance should be elicited Exhaustive inquiries of this sort should be directed to every other sensation naturally modifying the question according to the character of the sensations With the facts thus elicited a fair perception of the nature of the complaint will be acquired and the inquiry then should be pursued as to illnesses and habits of life that may have induced the complaint A brief inquiry into the functional efficiency of other organs as sleep the state of the digestion menstrual functions and frequency of micturition should be made

As distinct from these inquiries an inquiry must be made in all cases of heart trouble as to the efficiency of the circulatory system by getting from the patient the amount of effort he is capable of undertaking without distress as how far he can walk whether his work entails bodily effort and if so how it affects him what games he plays and how he bears the effort If there is a limitation of the response to effort the time it was first perceived and the attendant circumstances should be noted The nature of the sensations which limit the patients as breathlessness palpitation pain sense of exhaustion should be elicited From the character of these sensations we can gather whether the story of the patient is one of heart failure or of vasomotor disturbance

In children some difficulty may be experienced in getting out the facts but as a rule it is easy to appreciate the heart s efficiency when they are old enough to talk and run about Unfortunately there is a mistaken idea in the minds of parents and physicians that a suspicion of heart trouble demands that a child should be kept at rest No doubt in rare instances of *acute or progressive disease rest is necessary and the need for it may be* recognized by a physical examination But a great number of children who are supposed to have weak or impaired hearts and are able to run about are often needlessly restricted because of some physical sign murmur or irregularity It should be understood that children with a heart the efficiency of which is impaired will not injure it by overexertion Children are very sensitive to distress provoked by cardiac inefficiency and will themselves abstain without being told and one can usually recognize the degree of inefficiency by getting the child to state if he likes running about with a hoop or running up stairs When they say they like doing it and it gives rise to no distress it may be considered whatever the cause of the trouble that it has not impaired the heart s strength I cannot recall a single instance where I could reasonably attribute heart failure to a child s voluntary exertions

The same reasoning applies to the games of boys and girls when they exert themselves and find pleasure in doing so it may be taken for granted that no harm results

Affections of the Myocardium

In the description of heart failure it was shown that the efficiency of the circulation was dependent on the integrity of the heart muscle and that diseases of the other parts of the heart produced heart failure by embarrassment of the heart muscle It is not possible to give a description of any form of heart disease without understanding the condition of the heart muscle and this can only be perceived by the evidences of heart inefficiency although gross changes in the muscle may give rise to certain physical signs

In the vast majority of cases the myocardial diseases cannot be clearly differentiated and we are dependent for our recognition of them mainly on inferences drawn from the signs of heart failure The pathological conditions revealed post mortem usually show extensive changes in the myocardium more often of a fibrotic kind fatty degeneration of the muscle fibers being a comparatively rare condition Degeneration of the coronary arteries leading to fibrotic changes in the muscle is frequent in the elderly Sometimes we come across a case where death has ensued from heart failure with no naked eye or microscopic changes in the heart muscle which would explain the heart failure and one can only infer that the functional efficiency of the fibers was impaired

In the great majority of cases of chronic myocardial affection we are without any clue regarding the origin of the disease. We know that it occurs after rheumatic fever, and we infer that during the acute stage the myocardium may have been invaded by the organism that produced rheumatic fever. We can infer that a similar process occurs in other infections, and that after recovery from the acute stage a certain diseased state is left behind which ultimately leads to gross changes in the muscle wall. In the majority of cases we get no history of an infection to which we can trace the origin of the myocardial disease, but there is sufficient evidence to show that

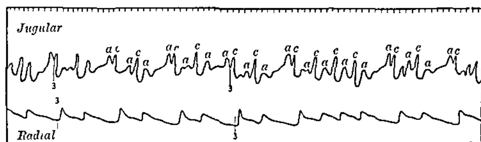


Fig. 1.—Simultaneous tracings from the vessels of the neck and radial pulse. The c waves are due to the carotid and are synchronous with the radial beats; the a and a waves are from the jugular vein and are due to the systole of the right auricle. It will be observed that the a waves are not followed by a carotid wave because the stimulus from the auricle does not always reach the ventricle on account of an impairment of the bundle connecting auricle and ventricle, thus giving rise to that irregularity in the action of the ventricle due to partial heart block. From a patient after typhoid fever.

many seemingly slight and trivial infections can invade the heart and damage it. Thus during or after an acute affection, as rheumatic fever, typhoid fever, or influenza, the appearance of an irregular rhythm may show that the auriculo-ventricular bundle has been affected, which may be taken as evidence of the invasion of the heart muscle. Figures 1 and 2, for instance, were taken from a man after an attack of typhoid fever. I have on several occasions detected the same phenomena during mild and severe attacks of lumbago or muscular rheumatism, and it is surmised that the fibrositis which affected the skeletal muscles also invaded the heart muscle.

The symptoms produced by a myocardium the seat of disease are identical with those produced when the muscle is weakened from toxic influences or poor nourishment, as in chlorosis and other anemias. This renders it impossible to say, in any given case, after a mild or serious febrile attack, whether the heart has been damaged. The long persistence of signs of cardiac enfeeblement may lead to the suspicion of myocardial damage, but beyond that we cannot go. For these reasons the symptomatology in the early stages is not distinctive, and the milder symptoms are dealt with in connection with exhaustion and the soldier's heart.

After the subsidence of the symptoms provoked by the acute or subacute process there may be a long period of seeming quiescence when the individual may pursue a strenuous life with no evident impairment of his powers In certain cases we can detect evidences of damage long before any noticeable failure of the heart appears as in the persistence of a wide a-c interval in graphic records from the jugular pulse evidence of a myocardial affection which has invaded the auriculo ventricular bundle The damage done to valves by an acute endocarditis is often progressive as shown by the gradual alteration in the character of the murmurs in aortic regurgitation

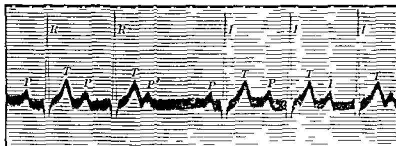


Fig 2 —Electrocardiogram from the same patient as gave Figure 1 The waves R and T are due to the systole of the ventricle The waves P are due to the systole of the auricles The waves P are quite regular but after the [illegible] waves P there is no ventricular response the stimulus from P being blocked Note the varying length of the P R interval

and mitral stenosis In many of the cases the myocardium is affected at the same time and here also the damage is not stationary but progressive Probably in every case of myocardial disease there is from the beginning a slight impairment of the functional efficiency of the heart shown by a limitation in the response to effort Unaware of this impairment the individual attempts to lead the life of a healthy person and the early symptoms of exhaustion are ignored The increasing ease with which these symptoms are produced directs attention ultimately to the cardiac impairment This recognition of the impairment may follow long after the original damage *the time depending naturally on the extent of the damage and the rapidity* of its progress and the amount of effort to which the individual has been subjected In addition to the changes induced by acute affections there is a series of cases where we cannot recognize the origin of the changes but find them associated with other conditions such as arterial degeneration high blood pressure kidney disease sometimes with a history of alcohol or syphilis These cases all pursue a similar course and show the same phenomena

It is almost universally assumed that the heart failure in people with valvular murmurs resulting from infection such as rheumatic fever is due to the chronic valvular disease and such cases are separated from those of heart failure with no murmurs the latter being described as cases of chronic myocarditis This distinction is scarcely justified for the valve affection has often little to do with the heart failure

Dilatation —The evidence of dilatation of the heart is made out by marking out the increased size of the heart I need not dwell upon how this is done for the methods for percussing out the heart s dullness are described in sufficient fullness in every handbook of physical diagnosis For practical purposes the transverse dullness at the level of the fourth or fifth interspaces gives on the whole the best estimate of the size of the heart In exceptional cases the whole area of deep dullness may be mapped out with advantage as when dullness is found extending to the left above the third rib In such cases the possibility of pericardial effusion should be kept in mind

It is very difficult to tell with certainty what share each chamber of the heart takes in the production of the increased size on account of the displacement of the whole organ The manner in which the heart is fixed above by the aorta the pulmonary artery and veins and the superior vena cava and below by the inferior vena cava keeps fixed an axis on which the heart to a certain extent rotates in the enlargement of its various cavities The tendency when the right ventricle dilates is for it to push the left ventricle to the left and behind with the result that in the great majority of cases of dilated right heart we get evidence of an extension of the dullness to the left and only a slight increase to the right When the right auricle becomes greatly distended it may push itself to the front of the chest and compress the right ventricle to a remarkable degree When there is extension of the dullness beyond the right border of the sternum it may with certainty be put down to the right auricle except in aneurysm or intrathoracic tumor

When the right ventricle enlarges it pushes the left ventricle further to the left and behind so that in great dilatation of the right ventricle the apex is formed by the right ventricle This can be recognized by the fact that the apex gives an outward thrust during systole when it is formed by the left ventricle and an indrawing during systole when it is due to the right ventricle (By the term apex I mean that part of the heart that beats lowest and furthest to the left) The epigastric pulsation due to the dilatation of the right side of the heart is also characterized by the indrawing during ventricular systole and the outthrust during ventricular diastole

When there is dilation of the left ventricle the outthrust of the apex may be felt as far out as the mid axillary line and in the seventh interspace

Hypertrophy.—The cause of hypertrophy is invariably an increased opposition to the emptying of the chamber. The systematic exercise of the heart's action keeps the organ in a healthy condition. A cessation of systematic exercise tends to diminish the vigor of the organ and even to produce atrophy of its active tissues. An increase in the exercise tends to produce an increase in vigor and an increase in the active tissues, so that within certain limits we may speak of a physiological hypertrophy, meaning thereby a state comparable to the large muscles of a blacksmith's arm. In such cases the hypertrophy is moderate and we no more get an abnormal hypertrophy of a healthy heart than we can get an abnormal expansion of the biceps as the result of exercise. This should be borne in mind, for there are certain terms often used which are misleading, such as that of "athlete's heart." This term is intended to denote an abnormally hypertrophied organ. I doubt if there is such a thing, and when my opportunities of observation are considered I think it will be allowed that I would have seen it if it had really existed. I have, on the other hand, seen many cases that were called "athlete's heart," but a careful examination of them invariably revealed other conditions which had been erroneously attributed to the athletics.

Setting aside, then, the hypertrophy which is physiological, all other forms of hypertrophy invariably occur as a consequence of some morbid condition obstructing the work of a chamber of the heart. The most extreme forms of hypertrophy are found with aortic regurgitation and adherent pericardium. There is something peculiar in the hypertrophy of aortic regurgitation, for though the muscle wall undoubtedly increases greatly in thickness I am not quite clear in my mind that the hypertrophy is an increase of healthy muscular tissue. In aortic regurgitation, if my doubts are justified, it is not therefore the obstruction to the output alone which causes the hypertrophy, for in aortic stenosis with no regurgitation, or with only a slight amount of regurgitation, we never see the same degree of hypertrophy. It is possible that the dynamic effect of the regurgitating blood may participate in the production of this hypertrophy, but so far as I have looked into the subject I have not found any constant correspondence between the degree of hypertrophy and the extent of the aortic leak. Moreover, the muscle itself is often so manifestly inefficient that one cannot but suspect that the hypertrophy is not genuine, even though the microscope reveals nothing but apparently normal muscular fiber. On this point, indeed, I cannot see a clear issue.

The same unsatisfactory conclusion is reached in regard to the hypertrophy of adherent pericardium. An adherent pericardium does not necessarily cause hypertrophy, because one often finds an adherent pericardium on the post mortem table when there is little or no increase in the size of

the heart On the other hand if the pericardium is more or less fixed to the chest wall in front to the ribs and behind to the spinal column *e g* in adhesive mediastinitis then the hypertrophy may be enormous To a certain extent this hypertrophy can be attributed to the fact that the muscle of the ventricle has to drag in the ribs during systole but I have found remarkable hypertrophy in cases of adherent pericardium of rheumatic origin when there was no attachment to the chest wall In these cases I fancy there has been some myocardial condition favoring an increase in the muscle wall but I have not been able to demonstrate it

Very big left ventricles are often found in kidney disease and in cases with persistent high blood pressure In these cases no doubt the arterial resistance is an agent in the production of the hypertrophy yet it is not clear that it is the only agent The conditions that affect the peripheral blood vessels affect also those of the heart itself and thus it may be damage the muscle fibers At all events I have been struck by the post mortem appearance of a number of my cases These hearts have shown towards the apex large areas containing but few muscle fibers and a great amount of fibrous tissue In these the muscle must have been seriously impaired years before the final breakdown

In dealing with the significance of special hypertrophies the matter must be considered along with the lesion producing them as in valvular disease A hypertrophy due to any morbid cause invariably indicates an inefficient heart There has come into use a term compensation which is employed in a manner distinctly misleading This term is often used in a vague and unscientific manner and those who use it rarely explain what they mean Thus we will find an individual with a murmur described as having a mitral leak with good compensation although his heart is perfectly normal and physiological in every respect A patient with orthopnea and dropsy from heart failure is spoken of as being in a state of "decompensation and when the dropsy has disappeared and the patient can lie down compensation is said to be restored though the patient s response to effort is permanently impaired

SYMPTOMS OF CHRONIC MYOCARDIAL DISEASE

The symptoms of myocardial disease beyond changes in the size and shape of the heart are revealed by changes in the rate and rhythm of the heart beat and there are always the signs of impaired efficiency which are those of heart failure already described In dealing in some detail with these latter phenomena it will be useful to separate them into two forms (1) those belonging to the second group of symptoms in the classification of symptoms *i e* the functional group where the symptoms are shown

in remote organs because the heart fails to maintain an efficient circulation and (2) those in which the symptoms arise from a stimulation of the central nervous system causing pain and allied phenomena The first of these forms will be described here the second in the chapters on cardiac pain

Rate—The rate of the heart in myocardial affections is extremely variable and is the variation in rate depends on so many factors it is not always easy to recognize the actual factor in any given case In some febrile cases a persistent increase in the rate may be taken as indicating the presence of some agent which either weakens the myocardium by injury (as the fibrotic changes in rheumatic affections) or by poisoning (as alcohol and the toxins of infectious diseases) In great exhaustion increased rate is frequently present and it may be that it is the increased rate which induces the exhaustion With extreme degeneration of the heart muscle the rate may not be altered

Rhythm—The different abnormal rhythms have a definite relation to diseases of the myocardium Extrasystoles auricular fibrillation auricular flutter irregularities and abnormal rhythms due to injury of the conducting system and pulsus alternans may all be the expression of an injured or impaired myocardium

Size—The evidence of hypertrophy of the left ventricle is mostly limited to the forcible thrust of the apex beat But though this is often a marked sign we not infrequently meet with a large forcible apex in very inefficient hearts with very extensive degeneration of the left ventricle The electrocardiogram may show a modified form when associated with hypertrophy of the different chambers and in its form indicate which chamber is preponderatingly hypertrophied A forcible shock is found inside the left nipple in hypertrophy of the right ventricle The pulsation of the liver due to the right auricle is suggestive of hypertrophy of that chamber induced by tricuspid stenosis Generally it is not possible to recognize the chamber or chambers which are most increased in size in dilatation or hypertrophy

Breathlessness—A deficiency of oxygen in the blood or the accumulation of certain waste products in the blood may stimulate the center of respiration to excessive activity Hence a weak heart that fails at any time to send sufficient aerated blood to the respiratory center induces breathlessness It may be that the heart cannot do this when the body is at rest giving rise then to orthopnea

Other factors may overstimulate the respiratory center rather than the failing heart as certain blood states the result of the anemias and diseased kidneys and mechanical conditions that interfere with the aeration of the blood in the lungs and disease of the lungs themselves

Breathlessness on Exertion—The most frequent complaint in heart affections is as we have seen shortness of breath which limits the patient s response to effort A limitation of this kind is not however peculiar to cardiac sufferers Many healthy people are short winded that is they have so little reserve force that their store is speedily exhausted What seems quite normal in them may on the contrary be due to some impairment in others Thus an individual who has been accustomed to take a considerable amount of exercise discovers suddenly a limitation of his powers This may be very slight and may not at first attract much notice Nevertheless the limitation may indicate cardiac inefficiency We have already seen that the amount of reserve force available varies in healthy people Bearing this fact in mind we shall not experience great difficulty in discovering by means of a careful appreciation of the patient s sensations whether the limitation is normal or is due to impairment

This breathlessness which arises as the result of effort is a symptom common to all forms of heart exhaustion slight and temporary as well as serious But it occurs also in other conditions—*e g* lung affections and exhausting illnesses so that no conclusion as to its real nature can be drawn until other phenomena have been investigated A weighing of the resulting evidence will reveal which of the many provocative causes is at work in the case of the particular individual under consideration

Breathlessness at Rest (Orthopnea)—When the breathing is labored while the patient is at rest so that he is compelled to assume a sitting posture the heart s impairment is so extreme that the reserve force is exhausted But before deciding that the distressed breathing is cardiac in origin we must exclude the various forms of respiratory disease which induce such extreme breathlessness—*e g* asthma pleurisy pneumonia emphysema and intrathoracic growth When due to enfeeblement of the heart the distressed breathing is generally the outcome of a long period of persistent overexertion The real cause of the trouble is thus insufficient rest In these cases the history may reveal the fact that the onset was gradual and extended over months or even years Rest in bed will often of itself restore a certain amount of strength to the heart and cause the breathlessness to disappear gradually When the breathlessness occurs rather suddenly the likelihood is that it has been caused by the heart taking on an abnormal rhythm for example auricular fibrillation, in which the ventricle is stimulated to rapid and irregular action Extreme breathlessness may set in within a few hours after the onset of auricular fibrillation though usually it does not appear for a few days or weeks

Cheyne Stokes Respiration—There is a type of respiration in which the breathing ceases for a short period (ten to forty seconds) and then gradually begins again from the period of cessation the breathing increases in intensity

till a maximum is reached and then gradually subsides until it ceases Sometimes these phases are very marked at other times they are so slight that they cannot be detected unless the patient is watched during his sleep The breathing known as Cheyne Stokes respiration may occur when the patient is sitting quietly in his chair usually at first it only occurs when he is asleep or dropping off to sleep Sometimes the patient passes into sleep during the apneic period and may resume a conversation when the breathing becomes reestablished Or he may continue to talk but in a faint voice during the apneic phase and return to his louder voice during the respiratory phase

Cheyne Stokes breathing is not usually discovered as a subjective sensation on account of the fact that many of those affected by it are quite unconscious of its presence Its presence may be suspected when the patient describes suffocating sensations which keep recurring when he drops off to sleep or states that he awakes feeling suffocated This sense of suffocation is usually due to recurrence of the apneic phase sometimes it is so distressing that the patient will suddenly spring out of bed in an extremity of terror

Cheyne Stokes respiration has a varied clinical significance Many elderly people with no particular disablement beyond the considerable enfeeblement so common in advanced years show it In people with high blood pressure advanced sclerosis of the heart and arteries it is generally a sign of approaching dissolution I have seen it in several cases of extreme heart failure with auricular fibrillation and auricular flutter and in these cases it had quite disappeared when the heart failure was relieved by digitalis

Cardiac Asthma —There is a form of dyspnea which comes on suddenly with great severity It is so often associated with marked changes in the heart that it has received the name of cardiac asthma although this is not a very good term as it tends to confusion with true asthma which has no association with cardiac disturbance It occurs most frequently in the night The patient goes to bed and may fall asleep for a few hours he is then awakened by a sensation of suffocation which forces him to sit up He breathes heavily and struggles to get into a position which will allow him to breathe with freedom This dyspnea may last for half an hour or longer and may then gradually subside so that the patient is able to go off to sleep again *Usually however the patient remains propped up in bed* and if he sleeps his sleep is troubled and disturbed with a fear of the recurrence of the distress The attacks resemble ordinary asthma and may be quickly relieved by a hypodermic injection of morphia

This condition occurs most frequently in elderly people with degenerated heart muscle high blood pressure and changes in the arteries These

conditions may also it should be noted occur in middle life and may be associated with albuminuria

Cardiac asthma is a very grave sign especially when it is associated with pulsus alternans and angina pectoris and is usually a prelude of death so that the duration of the individual s life can be reckoned by months in milder cases where the heart responds to treatment life may be prolonged for a few years

For some years I have been inquiring into the relation of this condition to Cheyne Stokes respiration and I find that the latter condition is present at times with cardiac asthma I find again that in most cases the patient wakes in distress during the apneic stage and the attack of severe breathlessness which then develops is identical with what is called cardiac asthma I am in consequence disposed to look upon Cheyne Stokes respiration as the origin of the attacks of cardiac asthma in all cases

Dropsy —Edema of the subcutaneous tissues is a common feature in heart failure with dilatation of the heart It begins first in the most dependent parts In people not confined to bed it is found first about and above the ankles in people lying in bed across the sacrum It may linger in the legs for years in some folks—worse towards night better in the morning In extreme cases it invades the thighs and abdominal wall The loose cellular tissue of the scrotum penis and vulva becomes infiltrated and the swelling may attain an enormous size Before marked effusion takes place in the abdominal cavity the bowels often become greatly distended with flatus The effusion may finally invade the pleural cavities producing hydrothorax The distended abdomen and the hydrothorax add to the embarrassment of the breathing If the patient leans more to one side than to the other in extreme cases the arm and cheek of that side may become greatly swollen

Associated with dropsy there is usually a diminished urinary secretion and disappearance of the dropsy usually coincides with an increased flow of urine

The significance of edema is extremely varied Many elderly people especially if they are stout may for years have their legs more or less swollen even if their hearts present no particular abnormality beyond a slight dilatation though it is more common amongst those with auricular fibrillation It may be present in attacks of heart failure to an extreme degree with ascites and hydrothorax and notwithstanding the patient may make a good and lasting recovery These are found more particularly in cases of rheumatic affection of the heart of some duration particularly with auricular fibrillation In this condition if the heart reverts to its normal rhythm the disappearance of the dropsy is more speedy than its onset If the heart reacts to digitalis the disappearance of the dropsy accompanie

the other beneficial effects of the drug When all attempts to restore the heart fail the dropsy increases embarrasses the heart and the respiration by effusion into the serous cavities and adds much to the suffering of the patient who drifts to a fatal issue

In extreme heart failure we may find a localized edema of one arm This results from the patient lying on that side If it is not on the side on which the patient lies then it is due to a thrombosis of the superior vena cava So extensive may this be that the clot may extend up into the jugular vein and along the subclavian into the brachial In such cases there will be no jugular pulsation on that side while it may be very marked on the opposite side

Dropsy and Dilatation of the Heart —One of the reasons inducing me to include dropsy as a symptom of dilatation of the heart is that I am doubtful if it is possible for dropsy to occur from heart failure without dilatation I see not infrequently cases of dropsy and enlargement of the liver diagnosed and treated for heart failure because there is a valvular murmur In these cases there has been no increase in the size of the heart and I have therefore assumed that the dropsy was not cardiac in origin The subsequent progress of the cases revealed that there were other causes for the dropsy (as cirrhosis of the liver or myxedema)

Enlargement of the Liver —Another result of the failure of the circulation secondary to dilatation of the heart is swelling of the liver from passive congestion It may not appear in the earlier stage in the first instance but when a patient has once recovered from an attack of heart failure with enlargement of the liver every subsequent attack induces this symptom sometimes before any sign of dropsy sets in

There may be associated with the enlargement a certain amount of jaundice and the combination of enlarged liver and jaundice with the wasting that sometimes accompanies long continued heart failure may raise the suspicion of malignant disease of the liver The dilatation or irregular action of the heart should direct attention to the real nature of the trouble

There may be a considerable degree of pain and cutaneous hyperalgesia associated with the enlargement of the liver The muscles of the abdominal wall may be contracted and hyperalgesic so that they embarrass the respiration

Edema of the Lungs —A symptom of great value is found in the careful auscultation of the bases of the lungs in cases threatened with some forms of heart failure as was pointed out in dealing with heart failure in the bedridden

Urinary Symptoms —I doubt if ever we get the characteristic urinary symptoms of heart failure in the absence of dilatation of the heart The c

symptoms are a scanty excretion increased specific gravity, and frequently the presence of albumin A diminished supply of blood to the kidneys may cause a large quantity of albumin to appear in the scanty urine as can be observed in heart block when the heart s rate becomes very infrequent The diminution of the quantity of urine excreted usually goes hand in hand with the dropsy The cause in the main is a fall in arterial pressure and a rise in the venous with consequent venous stasis in the kidneys Other conditions may cooperate such as the chemical constitution of the fluid in the tissues and changes in the secreting cells of the kidney It is often a difficult point to determine whether the albuminuria has been preexistent or whether it is induced by the venous stasis and subsequent inflammatory changes in the kidneys The history of the patient will help and the presence of arteriosclerosis and retinitis points to a preexistent Bright s disease It may be necessary to suspend judgment until a recovery of the heart restores the circulation as with the increase in flow of urine the albumin may entirely disappear

It is often useful to direct the patient s attention to the urinary excretion as its diminution may give the first warning of an impending break down and the increase in the flow is often the first sign of recovery of heart power

Heart Pain (Angina Pectoris)

When a healthy person runs until his heart becomes exhausted he is compelled to desist by breathlessness or a sensation of oppression across the chest sometimes accompanied by pain Pain can arise from the action of any muscle in health when that muscle is made to contract to an excessive degree or is forced to continue working after fatigue is produced When pain arises in a muscle affected by disease the symptom is produced in the same manner as in health only the exhaustion of which it is the evidence is more readily induced and the pain therefore appears with greater facility

If it is appreciated that the pain in heart affections is but a symptom which is capable of being evoked in all hearts the only difference between its appearance in health and disease being the greater ease by which it is produced in the diseased heart a good idea is obtained of the seemingly intricate and complicated phenomena which we call angina pectoris and which can therefore be looked upon as an expression of exhaustion of the heart muscle With this conception in mind we are put on a track which leads to a clear view of the patient s condition If in health exhaustion from overexertion induces pain in impaired health with a weakened heart muscle if pain is easily induced we are led to inquire into the cause of the premature exhaustion In people who suffer from any debilitating state

the heart likewise suffers and consequently in them we may get heart pain readily induced Although the heart pain may be a dominant symptom if we recognize that the heart condition from which it arises is provoked from some other source we are at once directed to search for causes that may tend to debility When extraneous causes of cardiac debility can be excluded consideration is given to the state of the heart as naturally a disease of the heart which impairs its functional efficiency will be apt to produce pain Here however we are met with a difficulty If a number of patients be examined who present different symptoms and their hearts are examined after death diseases seemingly identical may be found present in the heart Thus the coronary arteries may be found diseased with degenerative changes in the heart s muscle During life pain was the chief symptom in a few while others suffered no pain In cases of aortic disease pain is sometimes a dominant symptom while in others pain never occurs In the hypertrophied heart associated with kidney disease pain is occasionally a very distressing symptom while in others no pain is felt

That these differences should bewilder and confuse and lead to a great many theories as to the cause of pain in heart disease is but natural and we have many people who strenuously support this or that view and each supplies many facts which he claims support his view Some indeed would refer the pain to the state of the nervous system some patients having a nervous system more susceptible to pain than others and they have no difficulty in getting facts to support such a view

At this stage of knowledge it would be unprofitable to enter into a discussion of the subject We are far from having a clear conception of all *the facts that would enable us to explain the mystery of cardiac pain* Too little is known of visceral pain even in its simplest forms to enable us to understand all the factors concerned in its production But the fact is there before us of pain of a very distressing character which the doctor must do something to relieve while he may be unable to understand exactly how it is brought about While disclaiming therefore any intention of giving an explanation of how pain is produced in heart affections I propose to discuss certain aspects of the matter which have a bearing upon practice inasmuch as this gives a view which enables one to carry out measures of relief and affords grounds for rendering real benefit to the patients

The view that pain is an expression of exhaustion of the heart muscle gives the best idea of the nature and extent of the heart s impairment in grave affections of the heart as in milder affections The association of angina pectoris with disease of the coronary arteries is so well recognized that some take it as an evidence of coronary disease and the pain is supposed in some way actually to be produced by the artery itself If on the other hand we look upon the disease of the artery as preventing an

(in the upper arm ard l e ches) Wl en p in occurs in any part of the e regions the ques ion of i s being of cardiac origin should ari e In ome the pain may radiate to similar regions in the right side and in rare inst inces the pain is wholly right sided I have not been able to make out any pecu liarity in the heart that should account for the distribution of the p un on the right side In a few ca es the pain m iy also be felt along the lower jaw and behind the ears

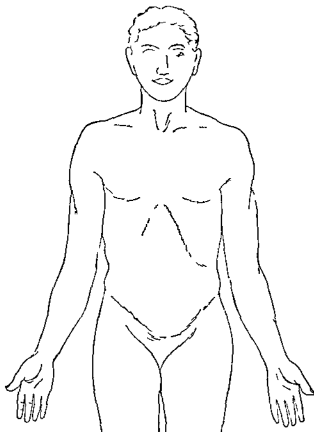


Fig 3 —1 he shaded area shows the situation of the pain an l l tribution of cutaneous hyperalgesia after the first attack of angina pectoris

The starting of the pain is usually acros the chest about the level of the third ribs or as low as the fifth ribs (Fig 3) It may how ever ari e in any part of the left side of the chest or in the upper or lower left arm When it starts in the chest it may remain fixed there but usually it spreads acro s the chest and into the left arm If it arises in the arm it spreads to

the chest After it radiates it remains fixed for a shorter or longer period with greater severity in one place either in the chest or in the arm

The duration of the pain may be for a few seconds yielding at once on the cessation of some provoking cause or it may remain for a few minutes or last with slight variation of intensity for many hours A dull aching not of much severity, may be present off and on for days An increased

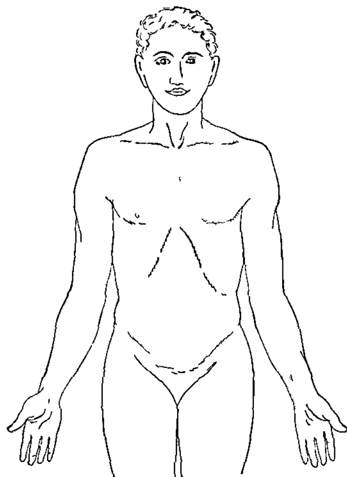


Fig 4—From the same patient as Fig 3 after repeated attacks of angina pectoris The pain and cutaneous hyperalgesia extended to the regions shaded here Note the areas in the neck and inner side of the left elbow

sensitiveness to pain (hyperalgesia) in the areas of skin over and around the left breast is often present in women The patient is sometimes conscious of this tenderness and any pressure hurts as when the clothing is rather tight It is elicited by lightly pinching the skin between the finger and thumb or by direct pressure with the finger Other structures than the skin are sometimes very tender as the pectoralis major muscle where it

forms the anterior wall of the axilla Here if one grasps the muscle the *pain is felt acutely* The *left sternomastoid muscle and the upper border* of the trapezius muscle are also frequently found to be tender on pressure Tender points may be found in the chest wall where branches of nerves are pressed upon and the lower cervical and upper dorsal vertebrae are also sometimes tender on pressure The hyperalgesia is not a frequent sign in men with severe angina pectoris but is common in the cases of debility due to some general toxic cause especially among women Its extent or intensity is not related to the gravity of the heart trouble

Associated with the attacks of pain are other reflexes the most frequent and the most instructive is the sense of constriction of the chest This may be limited to a slight uneasiness across the chest and it may never get beyond that Frequently this slight uneasiness gradually increases until the chest is held as if in a vise and the sensation because of its severity carries with it a sense of fear It is independent of the pain and may be present without the characteristic pain though both sensations are often combined I am disposed to look upon it as due to the violent contraction of the intercostal muscles resembling that contraction of the abdominal muscles so well known in diseases of the abdominal viscera A study of its peculiarities shows that it is identical with the spasm of muscles in pleurodynia It is of importance to recognize this sensation of constriction as it is often the first sign of the oncoming heart exhaustion In a large proportion of cases liable to severe attacks of pain as a result of effort the first sign that the heart is becoming exhausted is a slight sense of constriction When this occurs while walking if the patient slows his gait or stops the sensation at once disappears If on the other hand he ignores the sensation and *tries to walk it off it increases in severity and the pain appears and the* consequent suffering becomes so great that the patient is compelled to stop This severe stage may not be reached in the early days of the appearance of the signs but if neglected the exhaustion of the heart gradually increases until its neglect is followed by the greatest distress I will point out later how a recognition of this sign helps in treatment and in giving a guide to the patient in regard to the amount of physical effort he may undertake A curious matter in relation to this is that many men who have a tendency to angina pectoris recognize that this sensation of constriction is the same sensation which used to compel them to stop when in their youth they ran to the limits of their endurance so that its production in later years is but an indication of a greater limitation of the field of response to effort

Accompanying this sensation of constriction there is frequently a sense of suffocation a feeling as if the throat was being compressed and referred to the neck immediately above the sternum This sensation is I think

produced in the same way as that of constriction though I cannot make out the muscles that are affected

Other reflexes produced at the same time as the pain are occasionally present as a flow of saliva and increased urine excretion There is also often present that sense of collapse allied to shock if it be not the same thing as shock which results from a violent stimulation reaching the central nervous system by way of the cardiac sympathetic nerves

Pain and the other reflex phenomena appear in so many kinds of heart affections from those suffering from gross disease to others with healthy hearts temporarily exhausted, and we are so ignorant of many factors necessary to a full understanding of the condition causing pain that it is impossible to present the matter in a way that embraces the whole subject I think however the matter may be presented in such a way as will be found of great use in practice in separating for instance the grave from those of little significance and in obtaining indications for treatment

Recognizing that pain may arise from hearts affected by disease and in hearts in which there is no structural lesion but where the muscle is weakened by influences which produce exhaustion, as overwork poisoning or impaired nutrition we obtain a division which not only serves for a discussion of the subject but when the differences are appreciated places us in a position to diagnose correctly the great bulk of cases These two groups will be discussed under the heading of (1) angina pectoris from diseased hearts and (2) angina pectoris due to toxic and debilitating causes (see Chap XII)

Angina Pectoris in Diseased Hearts

The tragic circumstances associated with certain forms of angina pectoris have so impressed the medical profession as well as the general public that any suggestion of the presence of such a condition conveys with it a sense of grave danger That there are cases in which the occurrence of pain indicates a serious state is undoubted *but if it is understood that the pain is but an expression of exhausted muscle* and that in the vast majority of sufferers the exhaustion is not due to any serious form of disease a truer appreciation of the condition will be obtained Nor must the estimation of the gravity of any given case be based upon the degree of suffering for a severe *attack of pain is not necessarily dangerous nor* are the milder attacks free from a dangerous significance The importance of the symptoms must be estimated by an examination of the conditions that have provoked the exhaustion of the heart muscle To recognize that I have analyzed the records of many hundreds of cases and though the analysis *is not complete yet it has afforded a very safe basis on which a fairly* satisfactory prognosis can be given and a sensible line of treatment suggested

The division of the cases into the following groups afford a means of presenting the essential features of the great majority of cases

1 People in advanced life about fifty five and over in whom the changes in the arteries are leading to a deficient supply of blood to all the organs and in whom the arterial changes are more advanced in the heart

2 People in whom the arterial changes are proceeding in the heart with greater rapidity and the disease is not capable of being checked and a fatal issue speedily follows

3 People with damaged valves especially with aortic regurgitation

4 People whose hearts are embarrassed by having to labor against arterial obstruction as in chronic disease of the kidney with high blood pressure and with damaged arteries

5 A small indefinite group comprising rare conditions impossible to classify

Group 1 —Elderly people show certain signs which we recognize as being but manifestations of advancing years These changes present different features in many people In many the most evident signs are alterations in some portion of the circulatory system The skin for instance becomes thin and the capillary supply to the skin is greatly diminished The arterial walls become thickened and a cut made through the skin and subcutaneous tissues is not accompanied by that abundant oozing which we see in the young Rather it is more venous in character with spurting from a few small thick walled arteries These changes which are so evident in the external body wall take place in deeper organs and naturally impair their functional efficiency So far as the heart is concerned this is shown by an exhaustion of the reserve force shown by a restriction of the field of response to effort In some the exhaustion of the reserve force is manifested by breathlessness in others by pain

The pain in these cases does not come on all at once A man approaches his sixtieth year accustomed to a good deal of bodily exertion which in the past he has done easily and in comfort As time goes on there arises a feeling that the effort is not performed so easily as it used to be done He is more tired at nights or on going up hills there is a slight constriction across the chest which he ignores or tries to throw off by a spurt often he attributes it to indigestion For months this may disappear then it may recur and at last it may be after a long period of rather exhausting work or after some rather severe form of effort he is seized with a pain of great severity The attack may be of short duration or it may linger on for hours waxing and waning in severity If the patient and the doctor do not recognize the nature of the trouble and the patient resumes his ordinary life and exposes himself to fatigue these attacks will tend to recur and become easier of production until a period of rest is taken If the patient be

seen by a doctor who recognizes the nature of the trouble, simple modifications of the mode of life will enable him to resume his occupation and by living at a lower level he may lead a useful life for many years with no recurrence of the attacks On the other hand the patient may be frightened by being told he has 'angina pectoris' or the doctor may not use the expression for fear of frightening but hints vaguely at some obscure heart condition that compels restriction and a course of treatment and thereby reduces the patient to a miserable invalidism

There are certain features by which this group may be recognized and distinguished from the next group In both groups there is often no physical sign which throws any light upon the case and we have to depend entirely for information on the patient s description of his experiences It may be some time after the first attack or series of attacks before we can say definitely to which group he belongs This decision is arrived at by allowing the patient to get up and about as soon as he has recovered from the exhaustion that usually follows an attack He is permitted to walk so long as he feels no discomfort but as soon as he feels the slightest sign of discomfort in the chest as a slight constriction or sense of suffocation he is at once to stop It may be a few weeks or months before the tendency to the attacks disappears After that the recovery is generally so good that he can resume his old occupation By and by the patient will discover that the tendency is still present as some indiscretion in exertion will remind him of the trouble by the appearance of slight aching across the chest Moreover there are certain circumstances which favor the return of the pain such as walking after a meal or on going out on a cold day or walking against a cold wind In addition there are in some recurrent periods during which the attacks become easily provoked it may be when associated with some digestive disturbance In fact the close association of the attacks with flatulence often misleads doctor and patient as to the origin of the suffering and treatment directed to the stomach condition meeting with success in the sense that there is a temporary relief too often confirms the notion that the suffering is mainly digestive This also happens with the use of tobacco In some people liable to attacks of pain with structural changes in the heart wall the use of tobacco tends to provoke the pain and the assumption is that the tobacco causes the condition so we have the condition described as a "tobacco angina In all cases of this kind that I have watched sufficiently long the pain after a time recurred if the tobacco was stopped usually in response to exertion so that there is no doubt that in such cases there are actual changes in the muscle The position seems to be that in those predisposed to attacks of angina tobacco is one of the factors that tend to provoke attacks

In some cases belonging to this group the attacks of pain are at times

so easily provoked that the suspicion may arise that the disease is so far advanced that these belong to the next group The test I find most reliable is to recognize how much effort the heart can stand under the most favorable circumstances If the patient can walk several miles in comfort at any time then that is an evidence that there is still a good deal of healthy functioning heart muscle As years go on these people pass on to old age and suffer and *die from the infirmities which accompany old age sometimes from the* gradual exhaustion of the heart sometimes from a cerebral hemorrhage or more commonly from incidental illnesses as bronchitis or pneumonia

Group 2 —The degeneration of the arteries of the heart may proceed more rapidly and the heart s strength becomes reduced with greater rapidity than in the last group so that death follows much more speedily after the first appearance of the pain In the patients of this group the history of the pain shows that it becomes easier of production and tends to increase in severity from the date of its first appearance until it culminates in a series of attacks which call attention to the gravity of the condition In a few a period of rest may result in a long spell of comparative freedom but the attacks tend to recur with ever increasing ea e and the heart s strength becomes so exhausted that it is incompatible with life and the patient either dies suddenly during an attack or a series of attacks supervene and he gradually sinks

As a rule the signs appear earlier in life in this group than in the last in the late forties or early fifties The youngest age among my cases at which this pain appeared was a man of forty three and he died at forty six I am always anxious when men begin to complain of this pain before fifty years of age—not women for reasons I shall deal with later It is my custom in eeing this type of patient to insist on four or five weeks rest not confined to bed but mostly on the couch and be guided by the extent of improvement In a great many there are no physical signs and I have had several patients die within a few months of having their lives insured for large sums A careful inquiry elicited from the patients that they had suffered from indigestion which on questioning revealed the pain to be situated in the chest and arm (see Figs 3 and 4) and to be frequently provoked by effort

The post mortem examination in all the cases I have had the opportunity of making revealed an advanced condition of disease in the arteries of the heart with fibrotic change in the heart muscle One suspects syphilis as an agent but the majority of the patients deny ever having it and I failed to get any other evidences though I did not always use the Wassermann reaction

Group 3 —In this group the pain is as ociated with disea e of the aortic valves There is some peculiar relation of di ea e of and around the aortic valves to the nervous system and its reaction on the heart which has a very

important bearing upon the health of the patient We recognize the dilatation of the peripheral vessels as shown by the beating of the carotids and other superficial vessels and by the high systolic pressure and the low diastolic that gives rise to the Corrigan or water hammer pulse which is attributed to the regurgitation of blood back into the left ventricle during diastole Regurgitation is a factor in producing this characteristic pulse but it is not the whole cause for the dilatation of the arteries and the arterioles is brought about by the action of the vasomotor nerves There is in some cases an extraordinary sensitiveness of the vasomotor mechanism such as I have not found in any other condition shown by great variation in the blood pressure Thus a patient may be lying in bed and feeling quite comfortable but if disturbed or excited the blood pressure may speedily increase by 30 to 40 mm of mercury The curious fact that by the ordinary methods of blood pressure measurement in use the blood pressure in the vessels of the leg is much higher than that in the brachial artery suggests some factor difficult to understand provided that the methods employed are reliable

Another matter in this relation to the nervous system is the association of pain with aortic disease Though exhaustion of the heart produces pain associated with mitral valve disease the pain is not so frequent nor so severe as in aortic disease Here the attacks are often of the most painful kind and provoked in a peculiar way In some the pain accompanies the rise of blood pressure just mentioned and the patient may roll about in agony till it subsides Temporary relief may be obtained during the transient lowering of the blood pressure by one of the nitrites to return again as soon as the effect of the nitrite passes off In others the pain is provoked during periods of exhaustion such as occur with persistent sleeplessness Others occur at times from no apparent cause *e g* in men able to do heavy bodily work without distress as in a joiner I had under my care who usually suffered greatly on first getting out of bed but could follow his work all day without pain

These experiences relate to cases of long standing aortic regurgitation arising from rheumatic fever or syphilis or from those senile changes which damage the aortic valves Though in some cases the attacks of pain are indicative of approaching dissolution many live for many years after the appearance of the pain

In more acute affections of the aorta as in syphilitic aortitis pain of a very severe character may be the first indication that there is anything wrong and before there is much valve destruction death may supervene Pain arising in a young man with no demonstrable sign in the heart with a history of syphilis should always arouse the suspicion of an aortitis When accompanied by a regurgitant murmur the diagnosis is practically

assured and a serious condition recognized as calling urgently for the use of anti syphilitic remedies

The pain in aortic disease is so characteristic that eminent clinicians like Sir Clifford Allbutt consider that *the pain in all cases of true angina pectoris is aortic in origin*

Group 4—In this group where there is high blood pressure usually associated with or due to Bright s disease attacks of angina pectoris are apt to appear during the later years of life The condition is always well advanced and the heart s exhaustion extreme There is always considerable enlargement of the left ventricle and the arteries are usually thick and leathery and the arterial pressure ranges from 200 to 250 mm of mercury and over

I group these cases together because they have a correspondence and a resemblance in the stage in which angina pectoris appears in the sense that attacks of angina pectoris occur when the heart is so damaged that there is no prospect of recovery and when there is associated a series of phenomena which appear along with angina pectoris all indicating extreme exhaustion of the heart muscle such as Cheyne Stokes respiration pulsus alternans orthopnea and dropsy In some one of these symptoms may only be present and dominate the picture or several may appear together The previous history is very variable There may be a history of albumin in the urine for thirty years before any one of these symptoms appear On the other hand a patient may consult a doctor because of his being pulled up by pain or breathlessness on making some effort he used to do in comfort and the doctor finds a high blood pressure or slightly enlarged heart and no albumin in the urine In spite of all care and attention the patient develops albuminuria and Cheyne Stokes respiration appears and he drifts and dies within a couple of years after the appearance of his first symptoms On the other hand occasionally we come across a man about seventy with a blood pressure of 240 feeling fairly well who carries on in fair comfort for seven or eight years with little suffering beyond a tightness or slight pain across the chest on exertion till the later months of his life

The anginal attacks in these cases are therefore but one of the evidences of an advancing failure of the heart which we can do little to check

Group 5—In certain diseases of the heart attacks of angina may appear as in adhesive mediastinitis or other conditions whose nature may not be understood but which show signs of gross disease There are also met with in the course of years in practice attacks of illness of an unexpected kind which are so unusual that the doctor is often baffled to account for them Amongst my notes there are a number of cases in whom attacks of pain undoubtedly cardiac in origin occurred and presented features so unusual

that I am unable to explain them or to include them in any of the foregoing groups A man of a gouty habit had several seizures of severe pain in the chest and arms accompanied by collapse followed for weeks by a sense of prostration at the ages of forty seven and forty nine He quite recovered and led an energetic life and is today seventy three years of age and in good health

I was summoned in the middle of the night to see a man aged forty one suffering from severe pain across the chest with a sense of impending dissolution which was only relieved by a hypodermic injection of morphia He had not felt very well for a day or two before suffering from a tightness across the chest on walking but had thought little of it I could detect nothing amiss except a to and fro pericardial murmur which disappeared in a couple of days and the man made a good recovery and ailed nothing for many years after He died twenty four years later but I do not know the cause of death

A man fifty five years of age in good health, had been indulging in a series of dinner parties and after a rather Gargantuan feast was seized in the night by a pain of great severity over the chest and in both arms The pain was of a dull aching character and waxed and waned The patient could not sit still but kept shifting about to get an easy posture There was no sense of collapse The pain only yielded to a sedative (veronal) Next day the patient was quite well and suffered no more from heart trouble save that in later years he noticed occasionally a slight aching across the chest on going up hill but otherwise he is well and vigorous at the age of sixty six

A doctor aged fifty wrote me that he had a few attacks of great pain occurring when at rest The pain was typical of angina he said being situated across the chest and down the arms *At other times he felt quite* well and could play a round of golf with no distress Nothing could be detected amiss on examination I replied that there might be some infection present and after six weeks he wrote that he had another attack and for a few days there was a pericardial to and fro murmur which completely disappeared I saw him after this and he seemed quite well and was working hard A few months later he wrote to make an appointment to see me but telegraphed on the day of the appointment that he was too ill and wrote later saying that he had coughed up a large quantity of blood stained *frothy phlegm Two weeks later he died in an attack of suffocation*— edema of the lungs

Angina Pectoris in Its Relation to Sex

The vast majority of patients who suffer from angina pecto is due to actual disease as distinct from toxic or other debilitating causes are men

There are a goodly number of women met with whom one would put in Group 1 but exceedingly few in Group 2 In fact I only have notes of a few of this kind and they are not quite distinctive In aortic disease women are perhaps more liable to attacks of pain than men In the fourth group though high blood pressure is fairly common in women I have not seen many with the extreme form of heart failure Attacks of pain have not the same grave significance as the greater sensitiveness of the nervous system of women permits the appearance of sensory phenomena at a less advanced stage so that we get with high blood pressure cases in women who have slight aching across the chest with hyperalgesia long before there is any serious degree of heart failure

Conditions Favoring Attacks of Pain

While the immediate cause of the pain is dependent upon a variety of affections of the heart the circumstances that induce an attack are also variable To understand the matter it is necessary to recognize the extent to which the nervous system is involved That angina pectoris is the outcome of a stimulation of the central nervous system is so manifest that it needs no comment but it is necessary to recognize certain features which have an important bearing on the subject

Any condition which produces exhaustion of the heart also produces exhaustion of the nervous system and as the heart shows its peculiar evidences so the nervous system exhibits its own evidences of exhaustion One of these is an increased sensitiveness to stimulation This is typically seen in men and particularly in women who have suffered from conditions that have produced debility as overwork want of sleep or illness of any kind These people when they continue to make physical effort beyond a certain limit produce exhaustion of the heart and this is often accompanied by variable degrees of pain Frequently there is a persistent hyperalgesia of the skin a sure indication that some part of the central nervous system is in a constant state of increased excitability

This excitability can be inferred from other evidences A patient may have attacks of pain at first at rare intervals but by persistence in the cause that produces them as overexertion they become more frequent and easier to be produced In some sleeplessness produces such a degree of irritability that the attacks are produced by slight causes as exertion or excitement It might be said that this is due to an increase of the stimulus from the heart and implies a greater degree of exhaustion and in many instances this would seem to be true for towards the end of life the pain may come on with very slight provocation or no apparent provocation On the other hand one can in certain rare instances provoke the pain from

that I am unable to explain them or to include them in any of the foregoing groups A man of a gouty habit had several seizures of severe pain in the chest and arms accompanied by collapse followed for weeks by a sense of prostration at the ages of forty seven and forty nine He quite recovered and led an energetic life and is today seventy three years of age and in good health

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a stimulation independent of the heart. Thus in a boy with a greatly enlarged heart from adhesive mediastinitis the slightest stimulation of the skin under the left nipple would produce an attack. In another case a few days before death a patient could not raise his left arm without producing an attack, while he could raise his right freely.

The reason I dwell upon this point is that its recognition gives an indication for treatment, inasmuch as treatment directed to the nervous system rather than the heart sometimes affords relief.

Prognosis of Angina Pectoris

The view that angina pectoris is but the expression of an exhausted muscle and that the exhaustion may arise from any cause that overtaxes the heart gives a means for forming a fair prognosis in most cases. I have already pointed out that the estimation of the gravity of the case does not depend upon the violence of the symptoms. A severe attack is not necessarily serious, nor is the mildest free from danger. The importance of the symptoms must be estimated by an examination of the conditions which have induced the muscular exhaustion. This is, as a rule, not a matter of much difficulty if one searches carefully for a predisposing cause. The age of the patient, the conditions of his or her life, give a guide. If one has reason to suspect that the symptoms have appeared in the early days of advancing senile changes when the patient, ignoring the limitation of his powers, follows the mode of life pursued in the days of his vigorous manhood, then the probabilities are that with rest and care the heart will recover from its exhaustion and be able to carry on its work for many years in comfort but at a lower level. The prognosis is most serious where the attacks occur with marked evidence of general arterial and cardiac degeneration, where there is little response to treatment, and where the attacks are induced with very slight provocation. The presence of other phenomena, such as cardiac asthma, pulsus alternans and Cheyne-Stokes breathing, is an additional evidence of such advanced exhaustion that the outlook becomes very grave.

In all cases it is well to suspend judgment until a period of treatment has been tried, the treatment to include the suspension of all forms of effort which predispose to or induce the attacks. This is especially important where there is evidence of a progressive lesion in the heart, as in cases of syphilis affecting the aorta and its valves. If in spite of treatment the attacks recur with little provocation, then the outlook is very serious. Nevertheless there are cases so severe that for months a patient may scarcely be able to walk across the floor without inducing an attack, where rest for a long period may restore the heart's strength and induce a cessation

of the symptoms A helpful guide is to find out how much a man can do under the most favorable circumstances even though it may be but rare that he can do so much If he can at any time walk a few miles it means that he has still a fair amount of healthy muscle and it is so far a favorable sign

Treatment of Angina Pectoris

For the purpose of finding a rational therapy I include under this section all forms of pain and discomfort such as constriction of the chest sense of suffocation and sense of impending death which have their cause in some cardiac condition

Taking these symptoms as a basis we find they always occur in association with the exhaustion of the heart muscle whatever may have been the conditions which led to this exhaustion It is of importance to recognize this relation between angina and exhaustion for we are at once given a safe guide to treatment the practical indications being to restore the exhausted muscle and to prevent a recurrence of the exhaustion

But before dealing more fully with the treatment there is that other factor to be considered—the nervous system From a variety of unknown causes pain seems to be more readily provoked in some people than in others as shown by the fact that lesions apparently identical give rise to different nervous phenomena in different people Moreover as a matter of experience not only may pain be more readily produced in some people than in others but when once a tendency to attacks of pain is established the attacks become more easily provoked The recognition of this helps us in two ways first in recognizing the fact that the severity of the pain is no guide to the gravity of the lesion and secondly that treatment directed to the nervous system may be of far more benefit than when directed to an evident cardiac lesion We must then in any given case consider not only the cardiac cause of the exhaustion but also the part played by the nervous system in the production of the symptoms

In order to find out the best means of treatment we must seek for the cause of the exhaustion This is not as a rule a difficult matter and here I illustrate the manner in which this may be done

The most common forms of angina appear between the ages of fifty five and sixty five and in these case we have to consider what may have induced the exhaustion We know that in many people at this time of life changes take place in the circulatory apparatus which are due to advancing years aggravated it may be by the kind of life that has been followed We therefore carefully inquire into the life history and may find that the patient has been leading a strenuous life for a great many years doing as much as when in the prime of health and thrusting from him the indications

which revealed to him signs of heart exhaustion for if inquiry be made some symptom of discomfort as a slight tightness across the chest or *breathlessness has appeared at intervals long before the onset of the pain* which forced him to seek advice Manifestly the exhaustion here has been produced by a long continued strain and the possibilities are that after a period of rest the heart will regain a measure of strength and the distressing phenomena will disappear In such cases it is not necessary to stop a business man from doing all his work for to do so may affect his circumstances most seriously and his business affairs may be unnecessarily jeopardized It may be quite sufficient for him to omit some of his less pressing duties and the relief thus obtained may cause a cessation of the attacks

As a rule it is best for him so to arrange his affairs that he can take a restful holiday with his mind at ease The holiday should be spent in a manner which affords the maximum of enjoyment with the minimum of effort If the patient has no particular bent and would perhaps find a holiday drag wearily he might be sent to some watering place and made to undergo the régime peculiar to that place The carrying out of the directions would give his mind sufficient exercise to prevent tedium and he would have the opportunity of reaping what benefit the waters may possess In all cases the mode of living and the habits of the individual must be considered so that errors in diet abuse of alcohol or tobacco may be corrected There may be some valve defect (an aortic systolic murmur is very frequent) or a high blood pressure or thickened arteries may be detected While noting such conditions treatment should not be directed to their amendment for they are but associated phenomena and not amenable to treatment

In cases which do not benefit from such limited restrictions and when the attacks are demonstrably the outcome of an advanced exhaustion of the heart then more rest is required until in extreme cases it is necessary to confine the patient to bed In the more severe cases strict attention should be paid to the amount and kind of food and the state of the bowels freedom from annoyance and worry and a sufficient amount of sleep should be ensured if necessary by the use of hypnotics

It is only in rare cases that in spite of this line of treatment the patient gets worse the attacks recur and the patient finally succumbs *This* resistance to treatment is an important element in prognosis for it will invariably be found that the lesion which has induced the attacks of angina is of such an advanced nature that it has rendered the heart unfit to maintain a circulation compatible with life In such cases when in spite of rest and the correction of any errors in diet no progress is made and the attacks supervene on the slightest exertion we must recognize that we have

to do with an exhaustion so extreme that its cause may be due to organic changes in the heart muscle and that no prospect of recovery can be entertained Under these circumstances the patient must be kept at complete rest his food and habits carefully regulated and all circumstances likely to induce the attacks of angina avoided while sedatives such as chloral or opium may have to be administered to prevent the occurrence of the attacks or to lessen their frequency

But before coming to the conclusion that the heart condition is irremediable we must weigh carefully the possibility of the attacks being more readily provoked in consequence of an exalted susceptibility of the nervous system In many cases where the slightest exertion such as getting out of bed or walking across the floor may induce an attack if careful inquiry is made it may be found that the patient has passed through a period of stress worry or anxiety or may have had sleepless nights If such patients are protected from their worries and acquire peaceful restful nights recovery may at once set in and proceed to a surprising extent even when there is advanced degenerative change in the heart and blood vessels The most useful remedy in these cases is the bromide of ammonium given in doses of 1 3 grams (twenty grains) three times a day until a certain degree of lethargy and drowsiness is produced This remedy not only induces sleep but renders the patient more indifferent to the worries and troubles which may beset him In some cases there are periods when the attacks of angina are liable to recur and these are preceded by sleepless nights The administration *of the bromide when the sleeplessness first appears may prevent* the exhaustion which induce the anginal attacks

A very important factor has to be considered in treating cases with angina pectoris as well as all forms of neurotic heart and that is the mental condition The fact that patients who suffer from angina pectoris sometimes die suddenly or die shortly after the appearance of the symptoms has so impressed the lay mind as well as the medical that a very gloomy view of the condition is taken As a matter of experience it is only a very small proportion of the cases even of those with severe attacks in which there is cause for immediate concern The vast majority of patients recover to a very great extent and lead useful lives for an indefinite period We should therefore make a special study of each case and when we find the condition is not grave a favorable prognosis given with an air *of conviction* will at once do a great deal of good The element of hope must be based on a clear conception of the heart s condition and the careful physician will have little difficulty in detecting the essential feature in each case

In certain cases where there is aortic valvular disease attacks of angina pectoris are easily provoked and the patient s mode of life must be greatly

restricted on this account The attacks may appear in patients between thirty and forty where the valve disease was due to rheumatism or syphilis as well as in the elderly where the lesion may be due to fibrotic degeneration So severe may these attacks be and so readily provoked, that patients are forced to lie abed In such cases relief may be obtained by pushing the bromides 5 to 7 grams a day (one and a half to two drachms) until a condition of lethargy is produced and the patient lies in a drowsy condition After a few weeks if the patient is allowed to come out of the influence of the drug a distinct improvement may be found Such a patient is otherwise one of the most difficult kind to treat and is liable to become addicted to the opium habit when opiates are resorted to for relief Great suffering however is consistent with a long life and I have watched cases of this sort for twenty years

Treatment During Attacks—The slighter attacks require no treatment beyond the cessation of the exciting cause (such as effort) but when they become more severe rapidly acting vasodilators should be administered such as hot drinks hot water with whiskey or brandy and best and speediest of all amyl nitrite by inhalation or nitroglycerin The nitrites are not successful in all cases but often their action is rapid and the relief is generally complete When it is successful it is inferred that the patient has previously had constricted arterioles or increased arterial pressure and that the pressure was reduced and the heart was eased This is however not the full explanation A patient with cardio sclerosis had an attack of angina pectoris in my consulting room I took his blood pressure and found it 190 mm of mercury and then administered nitrite of amyl it acted instantaneously and gave him perfect relief After fifteen minutes I took his blood pressure again and found that it had risen to 200 mm of mercury Though the pressure was higher he had no pain

Oxygen inhaled during an attack may give relief When the nitrites fail to relieve the patient we are forced to use chloroform chloral or morphia in doses sufficient to give relief I have occasionally found that chloral acts beneficially not only in relieving the somewhat long attacks but in preventing the recurrence of the attacks particularly when given at night to induce sound sleep or when there are repeated attacks chloral in doses of 0 25 to 0 3 gram (four or five grains) given four or five times a day may produce a degree of drowsiness during which the attacks cease

Toxic Angina

Attacks of pain sometimes of great severity and alarming in appearance are very common among women who suffer from debility chiefly if not entirely toxic in origin These attacks are bewildering in their variety

and might be broken up into a great many groups The more I see of them the less inclined I am to refer attacks of pain in women to a serious condition of the heart I have laid it down for my own guidance that women who suffer from attacks of angina under fifty years of age with no demonstrable signs of gross disease of the heart (as aortic or mitral valve disease or great enlargement) suffer not from a primary heart trouble but from some condition which produces general exhaustion and the heart pain is but the expression of the heart exhaustion and serves as an indication to search elsewhere for the cause of the trouble I explained this view to a colleague one day and he said that he remembered in his boyhood that his mother when between forty five and fifty years of age suffered from attacks of angina pectoris of such severity that her life was despaired of but she had died at the age of ninety four

The circumstances which provoke the condition are described under exhaustion where it will be shown that during and after some infective process the circulatory and nervous systems are often temporarily affected The cardiac manifestations are variable palpitation and breathlessness being frequent signs while pain and other sensory disturbances are very frequent It is necessary to enter upon a description of these as frequently they are taken as evidence of serious heart trouble

The sensory disturbances arising in a toxic heart may be limited to a slight aching over the left breast with or without a small area of cutaneous hyperalgesia or there may be pain of the most agonizing description and a *widespread field of cutaneous hyperalgesia*

Many women complain of an aching in the left breast and pain on pressure and some may consult the doctor in the fear that these are signs of a cancer in the breast This pain and aching may be very distressing lasting for hours never attaining to a great severity but sufficient to cause such suffering and discomfort that their lives are rendered miserable This happens particularly among hard worked women with a large family or other dependents who require attention during the night so that the woman s sleep is broken and disturbed

The pain may appear only at periodic intervals and be of an agonizing description and indistinguishable from attacks of angina due to grave disease of the heart If the doctor takes into consideration only the attacks of pain he is liable to be misled If however he recognizes that the patient is a woman under fifty and there is no gross disease of the heart he will see the necessity for seeking for some cause of illness in other regions of the body The most common cause for this condition is found in the intestinal tract

If careful examination be made of the abdomen an area of hyperalgesia of the skin or deeper structure will often be found while a resistance

sometimes slight but quite distinct may be found in the muscles of one side of the abdomen A history of constipation can frequently be elicited and although the patients may declare that there is no constipation yet they will frequently admit that they have been conscious of slight pain and tenderness in some part of the abdomen usually in the right iliac region and they may say they have had attacks of appendicitis In the few cases that have been operated upon at my recommendation there was found in all a great many adhesions around the cecum An inquiry in which I am at present engaged reveals that adhesions here and in other parts of the intestinal tract are exceedingly common and are associated with or caused by stasis and decomposition of the intestinal contents Poisoning from other sources may give rise to very alarming symptoms as an accumulation of pus in some cavity such as the antrum or an abscess in the pelvis or elsewhere

While the character of an attack may resemble the attacks occurring in men with disease of the heart the manner of onset is usually different It may occur when the patient is at rest or on the slightest effort while at other times the patient may undertake considerable effort with no distress An inquiry into the previous history of the patient particularly with reference to the state of health in which the patient had been before the attacks appeared will afford ground for forming a safe opinion as to the gravity or absence of gravity in this kind of case

Another feature is that the pain is frequently not limited to the well defined area as shown in Fig 3 but may spread or be described as spreading around the whole arm and down into the abdomen Indeed the distribution of pain is like that of hysteria and many of these cases are described as hysterical angina pseudo angina or mock angina and in consequence the patients complaints are treated rather lightly particularly in view of the fact that none ever shows other signs of serious heart trouble But this view of the matter is not quite justified for I have repeatedly found patients labelled as hysterical or neurasthenic or hypochondriacal who were really in a poor state of health and suffering from some form of toxemia frequently intestinal The absorption of decomposing products from the intestine has an injurious influence upon the central nervous system and to pass these serious manifestations by as merely hysterical is to misinterpret their significance

Many men who have been exposed to toxic influences (microbic infection) and have been exposed to severe bodily fatigue develop similar symptoms Thus among soldiers exhaustion of the heart with pain and other sensory disturbance is not an infrequent occurrence Among these toxic cases are a number which have been described as vasomotor angina pectoris due to the fact that there is marked evidence of a contraction of the

peripheral vessels I have already dwelt upon this feature in angina pectoris in cases of aortic regurgitation but these toxic cases are of a different type although they have been mixed by some writers The idea that vaso constriction is a common cause of angina pectoris has gained ground but as a matter of fact it is of rare occurrence and certainly not the cause in the majority of cases

Many patients who suffer from angina pectoris experience an attack when they go into the cold air In them there are some organic changes in the heart and the increased peripheral resistance caused by the cold embarrasses and exhausts the heart or a constriction of the arterioles similar to what takes place in the skin may occur in the heart But there are rare cases in which the cold may induce such vasoconstriction that pain may occur in patients who do not suffer from gross disease of the heart but from a toxic condition Thus a patient aged thirty whom I had under observation for a number of years complained of the miserable sensation of exhaustion and chilliness which she experienced during cold weather On a few occasions she suffered from attacks of pain in the chest of which the following is an example On a raw November Sunday morning she went to teach in a Sunday school The room was cold and she felt chilly Still feeling chilly she went to church a cold damp building The sensation of cold got worse and towards the end of the service she began to feel a pain in her left chest This pain increased and on reaching home it became of great severity and extended from her left chest down her left arm She was put to bed with hot bottles and given hot drinks and when she became warm the pain subsided By taking precaution she did not have any more attacks

Prognosis—I have never seen a patient of this type suffer from any grave signs of heart failure although many live invalid lives for years due to the primary disease The outlook therefore depends on the possibility of the removal of this primary cause which if accomplished is speedily followed by recovery Otherwise the impaired health may persist for many years though some regain a wonderful degree of health after sixty years of age

Treatment of Toxic Angina—Recognizing the nature of the trouble the treatment is naturally directed to removing the cause of the impaired health and for this purpose a search must be made Even when not apparent at first the doctor should always be on the outlook for some source of infection and not infrequently some new development of signs will reveal the source though it may be after months or year

In addition to attending to sensible lines of managing the patient for the impaired health special lines of treatment may be required for the heart This is attained best by protecting the heart from exertion beyond

that which it can accomplish in comfort as by diminishing the amount of bodily effort and by securing sleep There are periods when the pain becomes easily provoked and besides rest at these times bromide of ammonia pushed until it produces a slight degree of drowsiness is often very beneficial When the patient feels this drowsiness then the drug should be stopped and resumed from time to time when the suffering calls for relief In this way the patients get to know when the medicine is required and can obtain relief until such time as the health is improved There is no fear of the drug habit being acquired as no patient ever has a craving for the bromides

Exhaustion, Palpitation, and Syncope

There are a number of people who suffer in many ways in whom one or more of the dominant symptoms are cardiac in origin and as a consequence these are often looked upon as cardiac patients and treatment is devoted to the heart while the trouble is really of a general kind and the heart condition is but a portion of a state in which most of the organs participate In producing this state a variety of circumstances take part the most common being some toxic condition which lowers the vitality as microbe infection or a chronic affection of other organs Superadded there may be persistent overwork worry sleeplessness and insufficient nourishment This subject is a large one and here I deal briefly with only a few of its more common aspects as they affect the organs of circulation namely with the symptoms of exhaustion palpitation, and syncope

Exhaustion

When exertion is made as in walking many people become conscious of a sense of weakness which causes them to desist The sensation is difficult to describe though most know from personal experience what the feeling is The chief element is a strong desire to stop and sit or lie down the legs feeling limp and powerless If the exertion has not been carried to an extreme degree the sensation quickly disappears when sitting or lying If exertion be persisted in the sensation may pass off in milder cases while in severer cases the individual may stagger and fall and even lose consciousness

Accompanying the feeling other symptoms may be present as breathlessness palpitation and pain over the left chest sometimes slight sometimes severe When these signs are present the patient associates the condition with the heart and the doctor may refer the whole train of symptoms to this organ particularly if there be present some abnormality or seeming abnormality as an undue increase in rate an irregularity a

murmur or slight increase in size It is because of this misconception that I deal with the matter for the sensation is not primarily a cardiac one though the heart may participate in the general weakness of which the exhaustion is the sign To bring out clearly its salient characteristics and how it differs from the symptoms peculiar to heart exhaustion certain of its features should be considered The sensation is usually not constant If provoked by exertion it will be found to vary from day to day or there may be *periods of weeks when the patient is free from it and then weeks* when it is easily provoked Some days if the patient walks a short distance as on a hot and close day too heavily clad the sensation is readily provoked on other days when the sun is bright the air cool and the individual lightly clad a wonderful amount of exercise may be taken without discomfort Certain other states besides exertion may bring it on as standing in a warm room Many women feel faint and exhausted when having a dress fitted or on raising their hands above their heads while standing and arranging their hair

To appreciate the nature of this condition it is necessary to search for other signs In many of those people who suffer from periods of exhaustion we find other abnormal signs referable to the vasomotor system Thus many will show changes in the peripheral circulation the hands and feet often becoming cold not only in cold weather but in response to some mental stimulus such as the excitement of being examined Many shudder at the idea of a cold bath as the after reaction is one not of a warm congenial glow but of a shriveled up cold feeling In some the fingers become pale and cold and the sensibility of the fingers will be so diminished that the fingers are numb At other times the hand and nose become red Some in a warm atmosphere become flushed and disagreeably hot Not infrequently pressure applied to the abdomen will cause the jugular veins to become full (see Fig 5) The blood pressure in these cases is usually rather low particularly during the attacks of exhaustion It may rise as soon as the patient lies down or after the exhaustion passes off and this accounts probably for the fact that sitting or lying speedily dissipates the sense of exhaustion

Taking all these facts into consideration I think we are justified in referring the state of exhaustion to a depletion of the higher nervous centers The vasomotor system is oversusceptible to stimulation in the one case producing an overaction a contraction of the vessel in response to cold in the other case a widening of the peripheral field from warmth or exertion In many cases the wearing of an abdominal belt that firmly grasps the abdomen will prevent the attacks of exhaustion and faintness

The heart is often irritable and causes a good deal of distress from attacks of palpitation or from extrasystoles In some it may dilate and

even show signs of insufficiency in the sense that effort may readily produce distress or discomfort from breathlessness or palpitation The mental condition may be affected irritability of temper and depression are not uncommon In many nutrition is impaired and these people become spare and thin The skin becomes dirty and yellow especially in the armpits and over the abdomen

It is not always easy to find the real cause of this condition although I think there is now enough evidence to show that in many cases it is due to some toxic influence A very considerable proportion of those who suffer so readily from exhaustion have distinct evidence of gastrointestinal troubles Many complain of different signs of dyspepsia and we can often detect evidence of stasis in some portion of the intestinal tract even when there

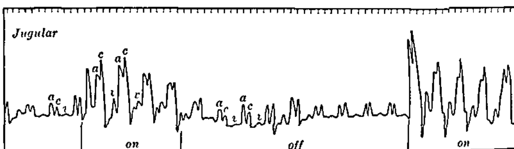


FIG 5—Tracing of the jugular pulsation when pressure is applied to the abdomen (*on*)—the jugular vein increases in size when the pressure is removed (*off*)—the venous distension diminishes

is no complaint made by the patient of indigestion Constipation is often present Many years ago I was struck by the disappearance of those characteristic vasomotor phenomena (cold hands and feet) in a man with a chronic duodenal ulcer on whom a gastroenterostomy had been performed

Although the absorption of the products of decomposition from the intestines is probably the most common cause absorption from other centers of infection is possible as from the teeth and obscure inflammatory conditions like chronic appendicitis A typical form is seen after exhausting illnesses such as typhoid fever or influenza In fact any prolonged bacterial infection may give rise to it

PALPITATION

The term palpitation is usually employed in a somewhat loose sense by patient and doctor As it is perceived by the patient and recognized as being due to some disturbed action of the heart it is only by *intelligently* questioning the patient that we can get the knowledge necessary to understand its nature except in those cases where we see the patient during

an attack The doctor interpreting the description given by the patient may bring out the fact that the condition is due to some abnormal rhythm as extrasystoles or auricular fibrillation subjects dealt with elsewhere The examination may bring out the fact that the heart beats heavily forcibly regularly with little or no increase in rate or with a considerable increase in rate and it is to these states I would restrict the terms palpitation and to which the following description refers

Palpitation may occur in relation to a great variety of complaints The patient is usually conscious of the change in the heart's action he feels the rapid beats and sometimes describes them as "gentle" sometimes as hard and hammering This latter sensation may occur with little or no increase in frequency In cases of valvular disease where there is a limitation of reserve force slight physical effort or mental excitement may readily induce an attack Even in the healthy certain mental states may have the same effect When the system is weakened from disease the liability to attack is naturally much increased It is in certain neurotic subjects particularly females that one sees the complaint attain its most distinctive features There may be no organic affection of the heart and though frequent attacks may ultimately induce exhaustion of the reserve force yet as a rule they do not appreciably shorten life Anything that startles the patient whether it be a sudden noise or mental perturbation or uncomfortable dreams readily induces an attack But an attack may supervene as the result of more obscure causes amongst which may be included reflexes from organs more or less remotely situated (stomach uterus) the source of the trouble may in other cases be indiscernible

When a severe attack comes on the patients may become painfully aware of the violent action of their heart They prefer to sit upright they draw deep inspirations and move uneasily from side to side with the hand pressed over the heart The attack is accompanied by sensations of a distressing nature such as a sense of suffocation and a fear of impending dissolution When it subsides it leaves the patient exhausted

During the attack the pulse is usually increased in frequency The artery may be of fair size sometimes however it is very small The impact of the pulse wave on the finger is sudden and sharp and of extremely brief duration

We occasionally meet with patients in whom the pulse is extremely rapid for a period sometimes for a few minutes sometimes for a few hours but who experience no sensation other than exhaustion and the attack quietly subsides The causes of these attacks are so obscure that it would be mere guesswork in the majority of cases to discuss them In patients with a high blood pressure attacks of palpitation at odd times in bed or on exertion or excitement are not infrequent

The opinion given by the doctor about these cases should be based in every instance on careful consideration of the cause of the irritation of the heart and inquiry must therefore be made into the patient's state of health and into the consideration of other organs, particularly those of the digestive system. The treatment is directed to the removal of any exciting cause or to the improvement of the patient's health as a whole. Where the patient is of a nervous temperament or where there is high blood pressure the judicious use of the bromides will help in diminishing *the frequency and severity of the attacks, especially of those attacks which* occur in the night. During the attacks relief is often obtained by drinking a cup of strong hot coffee or tea.

Syncope

Many people when placed under certain circumstances suffer from a diminished supply of blood to the brain and as a consequence the patients become limp and unconsciousness may result. This may result from the action of the heart being depressed by excess of vagal influence or from the stagnation of a large quantity of blood in the large abdominal veins. Abnormal actions of the heart as in the standstill of heart block or in the diminished output with greatly increased rate of auricular flutter may produce such a degree of cerebral anaemia that unconsciousness results. These abnormal actions are dealt with elsewhere; here the syncope due to vagal action and venous stasis will be considered.

Syncope from Vagal Stimulation.—When an impression is made by means of a violent mental stimulus, for example alarming information or the sight of some harrowing scene, a syncope may follow. Again violent intestinal peristalsis or severe pain, as for example that attending the opening of an abscess, may produce syncope. The patient becomes pale, beads of sweat may break out on the face and the whole body perspires, and as recovery takes place the patient may vomit. The pulse in such cases may become infrequent and of very low tension. Sometimes after recovery the patient may pass a large loose movement, indicating that the attack was probably the result of an intestinal stimulation.

Syncope from Venous Stasis.—Many young people faint when standing in a close atmosphere, e.g. schoolboys attending chapel; many women of anaemic flabby habit faint under similar circumstances; soldiers on the march, especially in hot weather, faint, probably because their heavy clothing keeps their bodies so warm that the peripheral vessels are dilated to such an extent that they deplete the brain. In some people the tendency of the blood to drain into the large abdominal veins is so marked that the fainting attacks are easily produced. Some of these people can be recognized

by the fact that if pressure with the flat of the hand is applied over the abdomen when the patient is lying down the jugular veins will be seen to swell up (Fig 5) This is an undoubted sign of the overfilling of the large abdominal veins as the pressure on them fills the right heart and the blood flow in the jugular veins is impeded In healthy people one gets no such reaction or only a very slight one while in those in whom the exhaustion is easily provoked the swelling of the jugular vein on pressure of the abdomen is sometimes very great I have seen one man in whom this tendency to exhaustion and giddiness was so great that he could not follow his work and was only comfortable when lying down A few minutes after standing up the heart raced off at a great rate and he became giddy and faint A firm abdominal belt at once produced such relief that so long as he wore it he was able to work Another man who consulted me staggered and reeled and sometimes fell on standing up He had made a habit of bending down and squeezing his belly before standing up I found that the pressure in the abdomen caused great fullness of the jugular veins

Syncope from these two causes occurs without any disease of the heart and the prognosis depends on other conditions which are present generally of a kind that tend to weaken the whole system While treatment should be employed to remove causes that tend to produce debility and to brace up the system by suitable measures much help may be afforded in those cases with stasis by exercises that strengthen the abdominal muscles and by the use of a suitable abdominal belt that can be adjusted so as to give a support without interfering with the free movement of the body

The Soldier s Heart

Exposure and fatigue during the war have impaired the health of many of the soldiers and among their ailments are symptoms which are generally attributed to affections of some part of the circulatory system While these conditions are not distinctive being indeed such as are common in civil life yet on account of the number that are affected and because of the difficulty in recognizing the nature of the trouble I give here a short chapter dealing with my own observations on the matter and the conclusions drawn therefrom which practically agree with the experiences of others who have made a special study of the subject In this reference to the soldier s heart I do not deal with the cases in which there was manifest disease of the heart as the principles of diagnosis and treatment in them are the same as in civil life

The description given of exhaustion corresponds to the symptoms present in the condition described as soldier s heart or the irritable heart of soldiers The British Government in 1864 appointed a committee

to inquire into the heart condition of soldiers as the condition we recognize today was the cause of much discussion at that time During the American Civil War the surgeons had ample experience of this trouble and articles published by Hartshorne and Da Costa are almost identical with the description which is given by the army doctors during the present war The subject was one that had interested me for many years and when the war broke out I seized the opportunity of making myself personally acquainted with the condition

In soldiers invalided because of heart trouble we find a good deal of variation in their appearance and symptoms The face is often lined and drawn many are spare and thin with a great vasomotor instability as shown by the manner in which the peripheral circulation varies the hands and fingers at times going pale and cold at other times the fingers are thick and red and the nose likewise becomes red and even blue with slight exposure to cold If they have been treated for some months by rest and feeding some become pale fat and scant of breath

The chief complaint is an absence of the feeling of being well they often feel out of sorts and a sense of fatigue or exhaustion easily induced is common to all Breathlessness on moderate exertion is frequent and more frequent is pain over the region of the heart The physical signs are variable The heart s rate is often not increased in some it is persistently increased as frequent as 120 per minute More frequently at rest the rate may be quite moderate but exertion sometimes slight may produce an undue rapidity

Murmurs systolic in time and heard in different regions are frequent while an increase in size usually slight is not uncommon In a few cases there is a slight edema of the legs

The mental condition is somewhat varied Periods of depression are not infrequent and the patients are often very irritable They accept the view that they have something wrong with their hearts and readily yield to all restrictions and are often content to lie in bed and brood over their woes These are the salient features in a great majority of cases We find identical condition in people recovering from an exhausting illness as typhoid fever or after a severe surgical operation We see all these phenomena well marked in people who are suffering from some microbic infection and we also find them in people who have suffered a long mental and physical strain particularly with insufficient sleep

The account given of the onset of symptoms is peculiarly instructive Some will say they were in the trenches and felt well and fit until one day they felt seedy and ill and this continued until they were compelled to seek medical advice when they were found to have a raised temperature A few days relief was obtained and they returned to their work still feeling

far from well and after a few weeks of the strenuous life in the trenches they collapsed sometimes with loss of consciousness breathlessness or even pain

The nature of the predisposing illness varies Sometimes it is an attack of diarrhea which persists for a time sometimes it is after a definite illness as measles but most give a history which we can safely surmise as being due to an infection In a few cases one cannot get such a definite account of the starting of the illness but many do recognize the gradual onset of the trouble That is the story of the majority of cases but there are a number from whom we can get no suspicious history of infection but where there is an account of a very strenuous life

To grasp fully how this exhaustion is brought about we must understand the life in the trenches The story of some of these soldiers is illuminating One in December 1914 suffered from appendicitis and was operated on He returned to duty three months after and in June went to the front Immediately on arrival he went into the trenches and was there a fortnight Every night was spent in repairing the damaged parapets They were constantly being shelled He never slept at night and often only got a few hours sleep in the day often being twenty four hours without sleep One day a shell exploded in the trench knocking him partly unconscious On regaining consciousness he stuck to his work for twenty four hours but had to give in feeling weak and ill with pain over the region of the heart

Effects of Strain During Infection —So great is the mental strain and bodily exertion with sleepless days and nights while the trenches are frequently bombarded that one might be disposed to consider that these factors would be sufficient to account for all the symptoms But we find identical symptoms present in many who have never been to the front and who have had no excessive bodily or mental strain but who have suffered from some febrile infection The majority also as I have said give a history of some previous illness and it is necessary that we should recognize the effect of strain or effort complicated by febrile illness For that purpose I recite the following experience

A young officer was training for a foot race and every day spent some time running round a track One day while doing this he collapsed fell and was picked up partly unconscious A doctor was summoned who said he had strained and dilated his heart and that was the cause of his collapse I was asked to see him and after getting this account I recognized that a man who had taken a considerable amount of exercise the day before could not possibly suffer from heart failure So I asked him if he felt quite well before he began to run and he admitted that he felt rather seedy but hoped to shake off the feeling with the exercise The temperature was taken and found to be raised a few degrees so I had no hesitation in stating

that the cause of collapse was the toxic influence of some microbe invasion and that after the subsidence of the fever and a few days rest he would be all right That is what happened, and he was able to resume his training and ultimately ran his race in perfect health

The action of toxins produced in the body by bacterial invasions has not yet been clearly worked out but so far as I have gone into the matter a clear and distinct group of illnesses can be attributed to the toxins even when the organisms themselves do little damage The phenomena I have described as characteristic of the soldier s heart give the idea of the point I want to establish that the condition is one of general exhaustion and the circulatory symptoms are but parts of a general manifestation Many people who ultimately develop some definite illness like consumption suffer in similar manner and the reason is probably the same a sense of weakness and ill health due to the invasion of the body by the tubercle bacillus before any physical sign is produced It is just possible that in some of these cases there is an actual invasion of the heart by some microbe and these symptoms may be the precursor of a chronic myocarditis but so far this matter is but a surmise

Treatment of Soldier s Heart

If we recognize the nature of the illness from which these soldiers suffer, we can readily see on what principles treatment should be based The lines are those we employ in civil practice If the patient be the host of some microbe the treatment should be devoted to increasing his power of resistance If he be poisoned treatment should be devoted to the elimination of the poison Should certain tissues be injured by the invading microbe or by the toxin or by physical strain then treatment should be devoted to their healthy renewal

These indications are practically those which should guide us in treating individuals after an exhausting illness We have however in addition to consider the mental condition of the soldier whose experiences have depressed his mental faculties and who has been told he has some heart trouble This knowledge always tends to depress and to make them extremely amenable to that form of treatment that is the worst for them rest in bed or the avoidance of exertion If we recognize that such cardiac phenomena as murmurs increase in size and variability of rate are but the manifestations of an irritated heart we shall see that too much rest is not beneficial Every organ benefits by the judicious exercise of its functions and the heart can also be beneficially stimulated

The principles of treatment then should be devoted to increasing the health of the body as a whole in such a way as to increase the natural

resistance to infection to eliminate toxic influences and brace up the whole man bodily and mentally The best way to achieve this is by fresh air and judicious exercise in the fresh air I need not labor the fresh air idea as it is evident to all but I want to emphasize the question of exercise

There is a notion deeply rooted that if there is anything wrong with the heart the patient must be restricted in the amount of effort and medical men who are themselves afflicted are quite content to lie in bed or move gingerly about The line I have adopted is to reassure the patients They often feel miserable so that there is a mental side to the case which is aggravated by the supposition that there is something amiss with the heart This aspect of the case has to be met and consequently in our treatment this view has to be kept in mind

When all fever has subsided or when there is but an occasional rise of temperature I encourage the patient to get up and go about I find out the form of outdoor exercise which gives him most pleasure so I recommend to him to start as soon as possible any form of sport or game which he can get fishing riding shooting golf etc

In recommending such exercise I have two objects in view The first is the mental condition of the patient and I need not insist upon the beneficial effects of occupation The more interesting that is the more likely is the patient to be taken out of himself I have referred to the fact that the sense of exhaustion is the predominant symptom in these cases and that it is probably vasomotor in origin due to the irritation of the central nervous system We know that the mental state may play a part in producing exhaustion for we find that a boring form of exercise will readily produce it while a form of exercise that is full of interest can be borne for long *periods without any exhaustion Therefore this out of door occupation* should be in an attractive form

In recommending effort I know it will be said that there is danger in this particularly when such physical signs as murmurs and dilatation are present If the true nature of these signs be recognized that they are but the expression of a temporary enfeeblement of the heart muscle and that the same measure for restoring a flabby leg muscle applies to a flabby heart muscle we shall see the importance of exercise judiciously employed No doubt injudicious exercise may do harm but there is one precaution of a very simple kind which suffices to prevent any danger and that is to instruct the patient to indulge in his exercise so long as it gives him pleasure and causes no distress nor discomfort but to stop or slow down as soon as he experiences a sense of exhaustion breathlessness or pain

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watched individual cases long enough to understand the significance of the murmurs the statement went forth with all the weight of the highest authorities that these signs betoken grievous heart trouble Today notwithstanding the enormous amount of attention which has been given to the subject the whole profession suffers from this untrustworthy observation Perfectly healthy men are rejected for the army or invalided out of it because a murmur has been detected in their hearts Others who present themselves for life insurance are rejected or made to pay a higher premium for the same reason while innumerable individuals are subjected to prolonged treatment and great restrictions in their mode of life because these early superficial observations have misled the profession At times physicians of experience will admit that certain murmurs may not have a serious significance in saying this many of them appear to imagine that they have made an important contribution to the subject But having failed to point out at the same time how a murmur can be valued so as to discover when it is of significance and when it is not they have really failed to carry forward our knowledge in any respect The result of this imperfect comprehension of its meaning is that at present every graduate leaves the hospital with but the vaguest notion how to assess the value of a murmur This confusion has arisen from the fact that the profession had not realized how the clinical value of murmurs should be assessed and in their confusion they turned their attention to devising new stethoscopes Thus we find for a great many years attempts were made in this direction and even to day the process goes on as shown by the introduction of the box stethoscope The result of all this expenditure of energy is that in essentials the knowledge of auscultation has made little progress during the last fifty years and what progress has been made has been by employing methods peculiar to clinical medicine and by using the simplest instrument the wooden stethoscope which indeed can scarcely be called an instrument as it is simply interposed between the chest wall of the patient and the physician s ear for the reason of cleanliness and convenience

In this account of the history of the stethoscope is seen the reason why the progress of medicine is hampered namely that it has not been understood how to employ methods in such a manner that will reveal matters essential to clinical medicine Instead of finding out the bearing that the cause of a murmur or a modified sound had on the patient s future the energies of the investigator were spent on modifying the instrument It is as if a poorly nourished individual was treated by modifying the spoon with which he was fed in place of improving the quality of his food This matter lies at the root of all investigation of medicine and it depends on the fact that for the advance of medicine methods are necessary which are peculiar to medicine No one however skilled he may be in other sciences

This simple and easily comprehended dictum contains in it the whole philosophy of the therapeutics of exercise as applied to the heart and may be used with safety in all obscure and doubtful conditions of heart weakness

Mechanical Aids in the Examination of the Heart

A conception has arisen among experienced clinicians that the limits of clinical examination by the unaided senses have been reached and that if advance in medicine is to continue new methods of examination must be devised They turn hopefully to the workers in other fields of medicine particularly to the laboratory worker and to the exponents of other sciences and these have responded to the call and there are now a great number of methods of examination which are employed as aids to the senses or as substitutes for them

A great deal of light has been thrown upon many obscure problems by the use of mechanical devices and other laboratory methods and this has strengthened the view that it is only by such methods that progress can now be made The employment of instruments of precision fosters the idea that medicine is becoming more scientific with the extension of their use and there is a tendency to rely more and more upon them and to substitute them for the senses of the physician I have little hesitation in saying that this attitude towards methods of examination which is dominant to day is based on a fallacy and so far from the clinical methods of examination by the unaided senses being exhausted they have not been sufficiently cultivated and the substitution of mechanical methods for them shows a lack of understanding of what clinical medicine means and how its study should be presented If the reader will refer to the classification of symptoms given at the beginning of this article he will find that it is absolutely necessary in dealing with diseases of an organ, to appreciate the functional efficiency of an organ and that there are symptoms which reveal this He will however understand that the symptoms revealed by mechanical device cannot do this for they all belong to the structural group This consideration reveals where the fallacy lies and shows that instruments can never supersede the intelligent employment of the senses

If we take the first of these instruments devised to aid in clinical examination the stethoscope we will see that the failure to realize the nature of the information it reveals has led the profession astray

About a hundred years ago auscultation began to be systematically employed in the examination of the heart With that injudicious enthusiasm which at all times has heralded a new method of observation fabulou qualities were at first attributed to the stetho cope People were found to have murmurs before their death hence before any single observer had

examination of the heart has ever thrown the slightest light on any cardiac condition. That the X rays may reveal aneurysms and tumors not perceptible to the unaided senses is no doubt true, but so far as the heart itself is concerned, while it may give a more accurate conception of the size of the heart in bulk, it gives no idea of the particular parts that are increased in size. Like the modification of the stethoscope, the modification of the X ray methods by orthodiagraphy and teleroentgenography has been of little practical use.

I am not in any sense decrying the use of instruments of precision. What I wish to point out is that they have but a limited sphere of usefulness in the examination of patients. The nature of the knowledge they reveal has been misunderstood, for we can now see the blunders that arose from attaching to the modified sounds of the heart a significance they never possessed, and the same untrustworthy method of estimating the significance of signs revealed by instruments is prevalent today amongst those who place their trust in their use.

The place these instruments should occupy is for the detection of obscure signs. The physician should then search for the associated phenomena that can reveal those signs by the unaided senses, so that these methods are useful in the education of the physician. Then they may be used when necessary for demonstration purposes, to present to the student an appearance by which he can verify the results of his examination by the unaided sense. They are also of use for purposes of research where obscure signs may be revealed and the progress of disease, or the effects of treatment can be studied.

It will thus be seen that for the routine examination of patients the trained physician rarely needs any of these instrumental methods. The essential features of a cardiac case can be made out by simple means, as by the intelligent questioning of the patient and by the use of his unaided senses in a physical examination. In fact, when one finds a physician employing a series of instruments for the examination of his patients, it may be taken for granted that he is in a rudimentary state of development and his powers of observation are likely to deteriorate for the lack of intelligent exercise of his unaided senses.

As an illustration of the limited and misleading information given by those who place their faith in instruments, the following is an example of great numbers of reports I have seen. The patient consulted me four years before because he had been alarmed by several doctors gravely shaking their heads over a murmur they had detected. The man was fifty six years of age, and had led a very strenuous life, and his appearance, though healthy, showed the outward signs of advancing years, grey hairs and lined face. He was, however, active and vigorous and capable of taking plenty

or in limited sections of medicine itself can understand or apply the principles essential to clinical medicine. What these principles are can be found out by finding an answer to the question "what effect has the cause of an abnormal sign on the patient's future?" To answer this question the physician has to watch the patient through the later years of his life as well as to search for the onset of the abnormal sign. This necessitates opportunities which are denied those who limit their observation to the study of disease in laboratories, hospital wards and the post mortem room. In thus watching the patient other methods peculiar to clinical medicine must be employed. In every case of impaired health a variety of symptoms is produced not only by the organ affected by the original disease, but by the effect of the functional derangement of the diseased organ on other organs of the body. We have, therefore, to employ the "law of associated phenomena" in determining the significance of any abnormal sign. The importance of this law and how it can be applied was demonstrated in the description of the manner of estimating the functional efficiency of the heart.

To employ this method of examination requires not a series of ingenious mechanical devices but a skilled physician who has obtained from experience a knowledge of the mechanism by which abnormal signs are produced, a knowledge of what will happen to the patient if the cause of the abnormal signs is left untreated or whether it is amenable to treatment, and this knowledge can only be acquired by a training of the senses.

Another outcome of applying the law of associated phenomena is that on the discovery of a mechanical method the senses should be trained to supersede the use of the instrument in place of the instrument becoming a substitute for the senses. This can be accomplished by recognizing the fact that an abnormal sign is usually perceptible in different ways. Thus an irregular heart recognized by graphic or electrocardiographic methods can also be detected by the peculiar sounds of the heart revealed by the trained ear or by the beat of the pulse revealed by the trained finger or by the movement of the veins of the neck revealed by the trained eye or by all three combined. While the nature of the irregularity was clearly revealed in the first instance by an instrument the systematic correlation of the signs revealed by the unaided but trained senses allows the instrument to be dispensed with.

In like manner the trained finger can estimate the character of the radial pulse and can give a better knowledge of essential matters than any blood pressure instrument or sphygmograph. The inspection and palpation of the movements of the heart and the percussion of the heart's dullness give a far more valuable indication of the size of the different chambers of the heart than an X ray examination. Indeed I am doubtful if an X ray

at a period when the cause of the sounds of the heart and much less the cause of the murmurs was not understood As years went on and investigation into the sounds of the heart ultimately brought out the true origin of some of these the inquiry into the cause of the different murmurs was diligently pursued and their origin at the different orifices gradually established Time after time physicians were able to indicate at which orifice a murmur was generated and confirmation of their predictions was found repeatedly at the post mortem examination It came to be looked on by the profession that murmurs were an evidence of disease of the valves As however many cases showed murmurs during life particularly systolic murmurs and the valves were found intact at the post mortem examination a functional" murmur was recognized But although these functional murmurs were not considered evidence of disease they came to be regarded as evidence of impairment of the heart s efficiency and as such to be indications for treatment and a restriction of the life of the individual

So deep an impression have modified sounds and murmurs made in the minds of the profession that a large proportion deem them invariably an evidence of an unhealthy heart the result of which is that we find every form of murmur looked on as an evidence of impairment if not of disease It is true that many physicians recognize and acknowledge that some functional murmurs may be harmless but when they attempt in their writings to deal with this problem their words convey so confused an impression that it is evident that they have but a hazy conception of the manner in which a harmless or physiological murmur is to be distinguished from a murmur which may be an indication of or associated with heart failure

The Sounds of the Heart

The first sound is produced by two factors the contraction of the ventricular muscle and the sudden stretching of the mitral and tricuspid valves Composed of these two elements it is subject to many modifications according to changes in the muscles or valves Consequently alteration in the character of the first sound is frequent and satisfactory explanations for these variations are not forthcoming Moreover experience has shown us that little can be made out of these modified sounds alone and while the modification should be noted the real opinion of the heart s condition should be based on other evidences which are never lacking A certain number of modified first sounds have gained a place in the terminology of cardiac affections and therefore need a brief reference

Feebleness or absence of the first sound may indicate extreme exhaustion of the heart muscle in the presence of other signs of heart exhaustion

of exercise without discomfort The increased size of his heart and systolic murmur were manifestly due to changes occurring with the progress of years, as indicated in Chapter III so I reassured him He kept well leading an active and energetic life till he was again advised to have his heart examined by the newer methods The following is the report sent to the doctor by the specialist who examined him It will be seen that no reference is made to the amount of effort the heart can stand and there is no estimate of the functional efficiency of the heart the most important of all matters in the examination while references are made to electrocardiographic appearances whose mechanism and prognostic significance nobody understands The use of such jargon only bewilders the doctor and impresses or alarms the patient

Pulse 92 per minute of normal volume and regular in rhythm no evidence of thickening of the vessel wall systolic blood pressure rather raised for his age being 162 mm on percussion left border of the heart about in the nipple line a well marked systolic murmur audible over the whole precordium and in the axilla its point of maximum intensity being at the apex

X ray examination of the heart shows the organ to be very horizontally placed left border one quarter of an inch outside the nipple line and transverse measurement at least seven inches thus considerably enlarged considering the age and build the aortic shadow is normal transverse measurement being two and three quarters to three inches The electrocardiogram shows left sided preponderance poor T deflections and inverted P s in Lead III

The poorness of the T waves indicates that the end of the ventricular contraction is not strong Considering how very horizontally the heart is placed I do not think the inversion of the P deflections is of any pathological significance In my opinion the organ is somewhat impaired and the affection is myocardial in all probability the result of the attack of pneumonia during youth

THE MODIFICATIONS OF THE SOUNDS OF THE HEART

Although I have already commented on the manner in which auscultation was employed when the stethoscope was first introduced the universal misconception of its use requires that attention should be called to the nature of information which auscultation reveals

Within a few years of the discovery of the stethoscope it was found that people who died from heart failure often exhibited murmurs of different kinds, and hence it occurred to the physician of that day that murmurs were manifestations of diseases of a serious nature This notion was taught

at a period when the cause of the sounds of the heart and much less the cause of the murmurs was not understood As years went on and investigation into the sounds of the heart ultimately brought out the true origin of some of these the inquiry into the cause of the different murmurs was diligently pursued and their origin at the different orifices gradually established Time after time physicians were able to indicate at which orifice a murmur was generated and confirmation of their predictions was found repeatedly at the post mortem examination It came to be looked on by the profession that murmurs were an evidence of disease of the valves As however many cases showed murmurs during life particularly systolic murmurs and the valves were found intact at the post mortem examination a functional" murmur was recognized But although these functional murmurs were not considered evidence of disease they came to be regarded as evidence of impairment of the heart s efficiency and as such to be indications for treatment and a restriction of the life of the individual

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Feebleness or absence of the first sound may indicate extreme exhaustion of the heart muscle in the presence of other signs of heart exhaustion

A flapping" first sound is sometimes spoken of as indicative of a thin walled ventricle but we must be chary of trusting to such a sign

A reduplication of the first sound may be due to a slight difference in the time of contraction of the two ventricles or at least to a minute difference in the times of the closure of the mitral and tricuspid valves Recently it has been found that a reduplicated first sound may indicate damage to the branch of the auriculo ventricular bundle leading to the right ventricle thus giving a lack of synchronism in the time of the contraction of the two ventricles

The second sound is valvular in its production An accentuation of the aortic sound is present when the aortic pressure is raised and the pulmonary second sound may be found slightly accentuated when there is engorgement of the lungs its cause is likewise due to increased pressure in the pulmonary artery

Reduplication of the second sound is loudest usually at the mitral area It is not clear how it is produced but it is so often present in mitral stenosis that its detection should always arouse the suspicion of stenosis of the mitral valve in the absence of more reliable evidence

A curious modification of the sounds of the heart is found when there appears a third sound interpolated between the first and second sounds The triple heart sound or gallop rhythm has been the cause of a good deal of controversy There appear to be different conditions producing it one of those is the reduplication of the first sound as already mentioned due to a lesion of the right branch of the auriculo ventricular bundle Some have looked upon it as a grave sign and no doubt it occurs towards the end of heart failure in such conditions as kidney disease but I have found it in individuals who were free from any cardiac lesion and who have lived for many years with no evidence of heart failure Muffled sounds seem to be of little significance ometimes they change into murmurs

Physiological and Functional Murmurs

There are some murmurs whose nature is so obscure that they are still the subject of discussion Some can with fair certainty be referred to definite orifices of the heart Organic murmurs are due to lesions affecting the valves and these can often be identified by certain peculiarities of the murmurs There are however murmurs which arise when there is no lesion of the valves these are spoken of as functional murmurs but many are really physiological in the sense that the hearts exhibiting them show no signs of failure during life The functional murmur usually occurs during ventricular systole and may be heard in various regions of the heart When heard loudest at the apex it is assumed to be mitral in origin when loudest

over the middle of the sternum it is supposed to be tricuspid in origin These murmurs are not infrequently heard loudest towards the base of the heart and it is difficult to determine in which particular region tricuspid *aortic or pulmonary they are heard loudest and it is sometimes suggested* they are cardio pulmonary in origin It is not possible in all cases to distinguish them from organic murmurs Much study has been devoted towards finding out if the mitral functional murmur could not be distinguished from the organic murmur because of its character and the regions into which it is propagated While many organic murmurs do show very characteristic features others resemble functional murmurs so closely that it is not always possible to speak with certainty

Functional murmurs are usually assumed to be due to dilatation of the heart rendering the orifices so wide that the valves fail to close them This is not entirely correct for while it is true that we may find a murmur with dilatation of the heart we may often find great dilatation and no murmur Further we find murmurs come and go when there is no perceptible change in the size of the heart the murmurs appearing only when the heart is excited or when the individual stands and disappearing when the heart quiets or the individual is at rest Again murmurs which we find when the heart is acting quietly with the body at rest may disappear on exertion or excitement

From this it can be inferred that there is some special mechanism apart from that involved in the dilatation of auricle and ventricle as a whole and this obscure mechanism varies under circumstances which we are still unable to appreciate The importance of this matter arises chiefly in connection with the heart of the young where it is probable that the heart has a peculiar power of adapting itself which is gradually lost in adult life It must be remembered also that free regurgitation can take place at the mitral and tricuspid orifices without murmurs We frequently get evidence of marked tricuspid regurgitation in the veins of the neck and in the liver with no tricuspid murmur

The chief importance attached to these systolic murmurs is that they are supposed to be due to blood escaping back from the contracting chamber This regurgitation has been assumed to be the chief factor in producing heart failure and from this conception has arisen the back pressure theory of heart failure There are no accurate data to show the quantity of regurgitant blood necessary to produce a murmur and we are forced to estimate *the amount by indirect methods I have been able to keep under* observation for twenty or thirty years individuals with loud rasping systolic mitral murmurs and who gave a history of rheumatic fever so that I could safely conclude that the murmurs were due to some damage of the mitral valves These patients never suffered from heart failure and I

venture the conclusion that in them the leak was small and the damage slight so that one may say within certain limits that in regard to mitral murmurs the narrower the orifice the louder the murmur Where there are functional murmurs the leak if there be a leak is so slight that it never embarrasses the auricles in their work apart from cases where there exists grave damage in the heart muscle The small quantity of blood thrown back does not alter appreciably the size of the auricles for we often find murmurs in hearts of the normal size

The Differentiation of Functional and Organic Murmurs

It is not always easy to distinguish between functional and organic murmurs As a rule *functional murmurs are systolic in time and are heard* loudest over different parts of the heart They are usually soft and blowing but these characteristics do not distinguish them from some organic murmurs Much has been written to determine the different features, but while organic murmurs often may be characteristic both in their character and propagation they resemble functional murmurs so closely that it is not possible in all cases to differentiate them A very rough murmur especially if accompanied by a purring tremor or a musical note is indicative of a valve lesion In the early stages however of an endocarditis the murmur *is usually soft and blowing resembling a functional murmur*

To distinguish between these two murmurs the whole circumstances of the case must be considered In the first place it is necessary to bear in mind that a murmur may be a normal event When we find a systolic murmur occurring in an individual in robust health with no other cardiac sign as a thrill or increased size of the heart we may consider it as indicative neither of impairment nor disease On the other hand when we find a murmur occurring in debilitated persons search should be made for conditions which account for the debility as anemia imperfect nourishment insufficient rest or disease of other organs It is of importance to differentiate these murmurs in febrile cases or after the subsidence of an acute febrile attack as after rheumatic fever The question then arises whether the heart has been affected by the disease process Here it is necessary to bear in mind that the raised temperature alone may produce changes in the heart's action such as increase in size and murmurs so that during the febrile stage of such acute illness judgment should be suspended until more definite signs of an organic lesion are forthcoming The persistence of a murmur after a febrile attack or its appearance should be considered along with the other evidences Thus after the subsidence of the fever if the rate becomes slow and the youthful type of irregularity is developed it may be assumed that the heart has escaped infection and that the murmur is

functional If on the other hand the rate is persistently increased then the fear is that the heart has become infected and that active changes are going on

The Significance of Systolic Murmurs

Seeing that individuals with systolic murmurs may be in perfect health leading strenuous lives and never show any sign of heart failure we may conclude that murmurs may be a physiological and normal sign and indicate no impairment of the heart s efficiency nor foreshadow the oncoming of heart failure

I wish to insist upon this fact for the possibility that a healthy heart may present a murmur is so opposed to the views of a great many of the profession teachers and practitioners that much harm is done to people who have to be examined for life insurance or for entrance to the services I base my views on the fact that I have watched numbers of healthy young people who exhibited this murmur grow up into manhood and womanhood and lead healthy and vigorous lives and never show the slightest sign of heart failure Moreover if we consider how little we know of the causation of murmurs it will be realized how little justification we have for treating them as abnormalities Even if they were due to regurgitation it is quite conceivable that the regurgitation might be consonant with a good functioning heart I have already pointed out that the fear of regurgitation has attained the dimensions of a bogy in the medical mind further I have already pointed out that even with organic disease the amount of regurgitation required to produce a murmur is very slight Functional murmurs may be present in debilitated individuals and in these cases the murmur is not necessarily an indication of disease or impairment of the heart nor is the valve incompetency which its presence indicates the cause of the debility Manifestly the murmur is then but one of the many symptoms which the individual may exhibit and the diagnosis of such cases will necessitate a search for other evidences which may throw light on the cause of the debility A systolic murmur may be present in cases of grave heart failure but in such cases the murmur is but an associated symptom for the valvular incompetence is not the cause of the heart failure but is merely one of the changes which have arisen in consequence of impaired functional efficiency of the heart muscle

The Significance of Organic Murmurs

Organic murmurs have a varied significance and it is necessary to grasp the idea that though murmurs are associated with heart failure the valve lesions which they indicate are in the most instances not the cause of it

It is also well to bear in mind that individuals with murmurs due to damaged valves caused by some infective disease such as rheumatic fever may lead vigorous lives and be engaged in strenuous occupations and never show any sign of heart failure. From this we can conclude that valve lesions in themselves may not necessarily be of serious significance. As however murmurs are often associated with heart failure the presence of organic murmurs should be considered from the following standpoints (1) as an indication that the heart has been invaded by a disease process (2) whether the damage done by the disease process is stationary or slowly progressive (3) whether the disease process has affected and impaired the heart muscle at the same time and (4) whether the damage of the valve is such that it obstructs the work of the heart so as to embarrass the muscle and impair its efficiency. In acute illnesses it will not be possible to answer these questions for there the immediate question concerns the acute affections. In chronic cases that is to say what is called chronic valvular disease it is absolutely necessary that these questions should be considered and answered if a rational conclusion is to be obtained. The manner of obtaining the knowledge necessary to answer these questions will be dealt with in the description of the different valve lesions.

The estimation of the significance of murmurs like all other signs should not be based on the murmur itself but on the functional efficiency of the heart and on the presence or absence of other signs of cardiac affections (size rate and rhythm). If we find in a heart of normal size and rhythm (or with the 'youthful type' of irregularity) a systolic murmur without any sign of cardiac inefficiency we may conclude that the heart is perfectly normal. If there be evidence of weakness or other signs of abnormal conditions present then the opinion should be based on these other signs and not on the murmur.

Diseases of the Valves

Tricuspid Insufficiency

John Hunter drew attention to the fact that in the normal heart the size of the tricuspid valves was not sufficient to close the tricuspid orifice. Since then other anatomists have also described this normal incompetency of the tricuspid valves and physiologists and others have found it present also in animals. In the routine examination of patients in health as well as when debilitated a systolic murmur presumably tricuspid in origin is not infrequent. The murmur is heard loudest over the sternum at the level of the third and fourth costal cartilages and is not propagated beyond the apex nor into the carotids.

I refer to this normal incompetence of the tricuspid valve because a false idea of the significance of tricuspid regurgitation has crept into medical literature which has led to a misunderstanding of the nature of heart failure and of the significance of the pulsation of the jugular vein and of the liver. This has arisen through the back pressure conception of the heart failure in which it was assumed that heart failure started by the giving way of the mitral valve which embarrassed the left auricle and the circulation in the lungs, followed by embarrassment of the right ventricle and giving way of the tricuspid valves, so that tricuspid regurgitation was supposed to be the

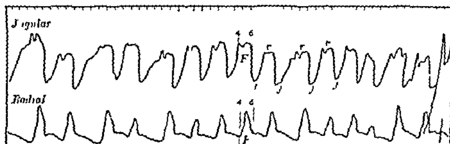


Fig. 6.—Simultaneous tracings of the jugular and radial pulses. The jugular pulse is of the ventricular type, there being no wave due to the auricle preceding the ventricular systole. The wave r occurs solely during the ventricular systole—space E. While tricuspid regurgitation is present, the peculiar significance of this form of jugular pulse is that it indicates the presence of auricular fibrillation, shown also by the characteristic irregularity.

last stage of this disastrous process and such signs as dropsy, enlargement and pulsation of the liver, congestion of the spleen and kidneys were supposed to be the outcome of tricuspid regurgitation. No doubt tricuspid regurgitation is present in such cases, but it has about as much to do with the causation of these signs as the spoon has to do with the nutrition of the body. Had physicians who have adopted the back pressure theory of heart *failure* but watched their patients as the phenomena arose, they would have observed that the result of heart failure frequently coincided with the symptoms of the condition now called auricular fibrillation, and the characteristic pulsation in the jugular and liver was an evidence of the appearance of the abnormal rhythm (Fig. 6) as shown by the disappearance of the waves due to the auricle, and by the associated disappearance of the presystolic element of the murmurs in mitral stenosis. These changes are shown semi-diagrammatically in Figs. 8 and 9. Although it is many years since I drew attention to these facts and pointed out though back pressure is no doubt one factor in heart failure, it is not usually a matter of much importance so far as mitral and tricuspid regurgitation is concerned, yet in recent literature I find the old descriptions given and even my own tracings of the jugular (Fig. 6) used as proving the presence of tricuspid

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that it caused the valves in the jugular and subclavian veins to close with a snap which I could hear over these veins as a clear sharp sound preceding the first sound of the heart

As a result of the stenosis of the tricuspid orifice the right auricle hypertrophies and on this account sends a wave back with such force that it distends the liver and therefore I look upon pulsation of the liver with a marked wave due to the auricle as suggesting the presence of tricuspid steno is

Mitral Regurgitation

Mitral regurgitation may be the re ult of a damaged valve or of dilata tion of the orifice from the giving way of the muscles supporting the valve The murmur of mitral regurgitation is systolic in time heard loudest at the apex It may be soft and blowing of little intensity and heard over a very limited area or propagated into the axilla or it may be rough and loud and heard over the whole heart and round to the back of the chest It is not always possible to tell whether it is due to dilatation of the orifice or to damage of the valves The rough loud murmur with an accompanying thrill is always a sign of damaged valves

When the muscle in unimpaired little or no bad effect follows incom petence of the mitral valves Even where the regurgitation is due to functional dilatation of the orifice the contractile power of the mu cle may maintain a good and efficient circulation and the patients enjoy perfect health with an efficient circulation The really serious trouble in connec tion with mitral regurgitation ari es when the muscle is impaired and the regurgitation may then add to its embarrassment Few symptoms of heart failure may be produced until the muscle gives way which is manifested by the signs of heart failure Dilatation is generally looked upon as the result of mitral regurgit ition the back pressure ultimately producing yielding of the walls of the right heart This is not quite correct for long before there is any back pressure we may find evidence of a dilated right heart If we examine carefully the condition of the heart when the valves have been damaged by rheumatic endocarditi during one of the slight attacks of heart failure which are likely to occur after overexertion we may find the heart slightly dilated the right ventricle being in front so that the left ven tricle is pushed to the left behind the lung the apex beat is then due to the right ventricle shown by an indrawing during systole After a few days rest and treatment the right heart may retreat and the apex beat is then due to the left ventricle the apex presenting the normal characters—an outthrust during systole In such cases there is no evidence whatever of pulmonary engorgement and back pressure In fact where there is heart failure Graham Steel says the change in the valves is altogether

regurgitation while the real significance as demonstrating the presence of auricular fibrillation has been lost sight of

When the auricle is active with tricuspid regurgitation the jugular pulse is not of the ventricular type, but is of the auricular type, as is shown in Fig 7 It is only when the auricle ceases to be active that the ventricular jugular pulse appears (Fig 6) It will thus be seen that tricuspid regurgitation is of little practical importance when a systolic murmur is perceived and the extreme signs of heart failure are not brought about by the tricuspid regurgitation but by the failure of the heart muscle to send the blood around

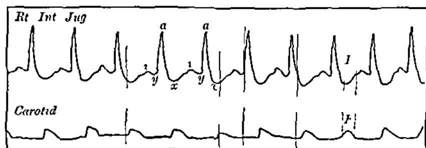


Fig 7—Simultaneous tracings of jugular and carotid pulses The jugular pulse is of the auricular type there being a large wave *a* due to the auricle (Compare with Fig 6) In this patient the tricuspid valves were partially destroyed and the orifice was incompetent so that there was free tricuspid regurgitation showing therefore that tricuspid regurgitation does not of itself produce the ventricular type of jugular pulse

the circulatory system with sufficient force It must not, however be assumed that tricuspid regurgitation is not present in the absence of a murmur for we will often find a jugular and liver pulse of the ventricular form without a murmur and at the post mortem a greatly dilated tricuspid orifice may be detected A weak muscular wall and a wide orifice may give rise to no murmur

Organic lesions of the tricuspid valves are rare and are nearly always associated with similar lesions in the mitral and aortic valves The heart failure associated with these lesions is never due to the tricuspid lesion alone

Tricuspid Stenosis

In the majority of cases tricuspid stenosis is not recognized during life as the symptoms produced are not always distinctive It is only rarely that a presystolic tricuspid murmur is heard I have only heard it in three cases in which it was present in a very limited area over the middle of the sternum There is usually present also a mitral presystolic murmur at the apex but as each murmur is confined to limited regions I have had no difficulty in distinguishing them In one case the auricle had become so greatly hypertrophied that it sent back a large wave into the jugular and with such force

fibrillation thereby profoundly affecting the efficiency of the heart and modifying the nature of its rhythm

From this it can readily be understood that the manner in which heart failure is brought about is somewhat complicated In some embarrassment may not ensue until the narrowing of the orifice has become extreme In others there may be a fatal issue while the narrowing is yet moderate In the latter cases the muscle wall inevitably will be found to have been damaged

The murmurs present in mitral stenosis the presystolic murmur or the auricular systolic are due to the contraction of the left auricle forcing blood through the narrowed mitral orifice With the advancing cicatrization the murmurs of mitral stenosis alter and present peculiarities that hitherto have not been sufficiently appreciated In the very early stages some years before the appearance of a murmur I have detected a slight presystolic thrill The first murmur to appear precedes or runs up to and seems to terminate in the first sound and is audible over a small area around the apex At first it may not be always present This murmur may vary in duration being usually short and abrupt but it sometimes begins earlier and is somewhat prolonged It is of a crescendo character rising in pitch till it ends in the first sound

With advancing stenosis of the orifice another murmur makes its appearance namely one occurring immediately after the second sound heard only in the immediate neighborhood of the apex beat At first it is very faint and not very constant but it usually increases in duration until the whole diastolic period may be filled up by it This diastolic mitral murmur diminishes in intensity from the beginning differing thus in its diminuendo character from that of the presystolic Frequently we can detect a continuous murmur during the diastole of the heart beginning loudly falling away then increasing in intensity The first or diminuendo portion of such a murmur is the diastolic mitral murmur while the terminal crescendo portion is the presystolic The cause of the diminuendo diastolic mitral murmur is the flow of the blood that has been accumulated in the auricle during the ventricular systole through the narrowed mitral orifice this begins as soon as the mitral valves open that is when the pressure in the ventricle falls below that in the auricle The development of these murmurs is shown in Fig 8

The next change in the character of these murmurs is the sudden disappearance of the presystolic crescendo murmur while the diastolic murmur persists Usually this change occurs with the onset of grave symptoms of heart failure the heart's action becoming rapid and irregular At other times the change takes place with no serious symptom but the heart invariably becomes irregular This is due to the fact that the rhythm of the

inadequate to explain the evidently free regurgitation that occurred during life and the disastrous dilatation of the heart The muscle failure factor it may be presumed was the essential one"

The damage to the valves is most commonly the result of rheumatic endocarditis and as we have seen the process is rarely limited to the endocardium but invades the myocardium Septic endocarditis may also damage the valves In all cases of mitral stenosis there is mitral regurgitation but the amount of the regurgitation is never so marked as to be the serious factor in the case

Regurgitation occurs through the mitral orifice with the valves uninjured in the later stages of many affections such as conditions that produce exhaustion of the heart muscle but more particularly in renal disease and cardiosclerosis Here the condition is brought about by the failure of the muscle to support the orifice and this may be one sign of a final and fatal exhaustion of the heart muscle

It will thus be seen that the symptoms produced by mitral incompetence are only of gravity when there is also muscle failure and this is dealt with in sufficient detail under affections of the myocardium

Mitral Stenosis

This is perhaps the most common of valvular defects with which heart failure is associated It arises generally in consequence of rheumatic endocarditis though it may be found in people with no rheumatic history and a previous history of erysipelas or some other febrile complaint may give a possible clue to its origin

The condition is never recognized during the acute process which induces it for the reason that stenosis does not occur till the cicatrizing process following the inflammation narrows the orifice and on account of its origin in scar formation it is often a progressive lesion Once the stenosis is present it may remain moderate in amount and offer so little embarrassment to the heart that patients may reach extreme old age with no heart failure As a rule however the cicatrizing process goes on with varying rapidity until in some cases the mitral orifice is reduced to a mere slit and the valves resemble a thickened calcareous diaphragm It is important to bear in mind the progressive nature of the lesion for it accounts for the varying changes in the symptoms It should also be borne in mind that a similar cicatrizing process may be going on in the muscle, causing contraction of the chordae tendineae impairing at other places the functional activity of the heart muscle and affecting the auriculo ventricular bundle depressing the conductivity or producing the conditions which lead to auricular

rest this exhaustion may disappear and the patient may go on for years with little further trouble After a time however some again break down and the symptoms complained of may be of the same nature Frequently however a change is found in the character of the murmurs a diastolic murmur usually being perceived and there is sometimes a longer duration of the thrill these signs implying an increased narrowing of the orifice On the other hand in those in whom no further narrowing takes place the murmur does not change and the patient may go on for many years and

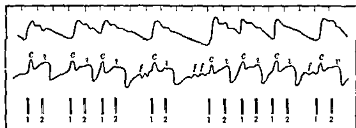


FIG 9 —After the changes described in Fig 8 the next change is a sudden alteration of the rhythm of the heart In Fig 8 the heart is quite regular in Fig 9 it is irregular The wave *a* which is a marked feature in the jugular tracing of Fig 8 is absent in Fig 9 The presystolic portion of the murmur is also absent in Fig 9 this feature being best appreciated during the longer pauses The disappearance of these evidences of auricular activity and the irregular action of the heart indicate the onset of auricular fibrillation The waves *ff* are due to the fibrillating auricle

if a female she may bear children with no breakdown In these cases we can infer that there is no progressive muscular or valvular sclerosis With the increased narrowing of the orifice as indicated by the appearance of the diastolic mitral murmur the heart becomes much embarrassed the symptoms become much more distressing and finally dilatation of the heart may set in But even without the progressive narrowing dilatation may appear early and then it may be inferred with certainty that the rheumatic process has permanently injured the heart muscle It is to be noted that frequently the left ventricle also dilates showing that there is some vital *factor concerned in dilatation*

The rhythm of the heart may become continuously irregular with the onset of auricular fibrillation and further embarrassment arises If there be no change in the size of the heart with auricular fibrillation and no great acceleration of rate the heart failure may be very slight in degree but if the heart dilates especially if the rate is accelerated then all the extreme symptoms of heart failure follow (dropsy enlargement of the liver etc)

In the vast majority of cases the heart recovers from its first break down and usually from many subsequent attacks Indeed after one attack I have known patients go on for twenty years and more with no further trouble beyond a slight limitation of the field of response to effort

heart starts no longer with an effective auricular systole but the auricle ceases to contract as a whole being in the condition of fibrillation (Fig 9)

When the heart's action is slow there is no difficulty in recognizing the diastolic murmur and the absence of the presystolic The diastolic murmur is sometimes of great length starting immediately after the second sound *and when the heart's action is rapid it may fill up the whole diastolic* pause, and it might hastily be assumed that the murmur was presystolic But if the heart be carefully auscultated it will be found that it is not

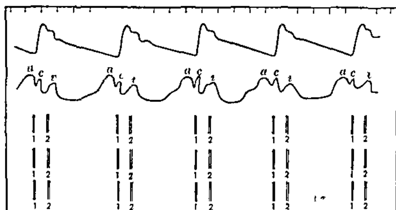


Fig 8 —Tracings of the radial and jugular pulse with diagrammatic representation of *the changes in the murmurs of mitral stenosis The down strokes 1 and 2 represent the* first and second sounds of the heart The first indication of stenosis is the appearance of the murmur before the first sound and on reference to the jugular tracing this murmur will be found to coincide in time with the wave *a* due to the systole of the auricle With an increase in the stenosis a short diastolic murmur appears immediately after the second sound and this is represented in the middle diagram A further increase in the stenosis shown in the lowest diagram leads to prolongation of the diastolic murmur which in combination with the presystolic murmur fills up the whole interval between the second and first sounds (For the next change see Fig 9)

crescendo in character when a longer pause occurs it will be found that the murmur stops short before the first sound so that there is a silence between the end of the murmur and the first sound (see Fig 9) In these cases the jugular and liver pulses are invariably of the ventricular form From the progressive nature of the lesions in the valve and in the heart muscle it will be realized that the symptoms are not constant The patient comes first into consideration mostly in early or middle adult life The complaints then are shortness of breath a sense of suffocation and palpitation on exertion In some the face is ruddy, with a hue a shade darker than is compatible with the ruddy countenance of robust health in others there is pallor At this stage there is little or no increase in the size of the heart and no dropsy A presystolic murmur can usually be detected The patient's complaints may be the only evidence we have of the heart failure and these point to an exhaustion of the reserve force After a period of

fibrillation the patient may make a good recovery especially if the heart is susceptible to digitalis In rare cases the curious and usually fatal condition suffocative edema of the lungs may unexpectedly occur

Vegetations may grow on the mitral valves with no certain sign of their presence until a small portion is detached and impacted in some vessel gives rise to a hemiplegic attack or an attack of aphasia Usually recovery takes place speedily and may be permanent but cases have been recorded in which the aphasia or hemiplegia has remained complete for many years Clotting may occur in the auricular appendage during auricular fibrillation and be a source of embolic infarct

Attacks of angina pectoris although very rare may occur in mitral stenosis In the few cases I have observed they were all secondary to

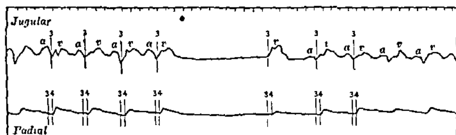


Fig 10—Simultaneous tracings of the pulsation in the jugular at the same time as the radial showing the temporary arrest of the whole heart from digitalis The first beat after the long pause is an escaped ventricular beat there being no auricular beat preceding it The waves a are due to the auricle and the waves v are due to the ventricle

some excessive exertion and the patients had only one or two attacks remaining perfectly free from them for years afterwards

Aortic Stenosis

Aortic stenosis is often associated with aortic regurgitation and the symptoms of the latter usually dominate the situation When there is little or no regurgitation the murmur of aortic stenosis may only be detected in the routine examination of the patient

Aortic stenosis which embarrasses the left ventricle is by itself a rare condition I have only seen it in a few elderly people in whom there was a syphilitic history A systolic murmur at the base of the heart should never be taken as indication of aortic stenosis without other characteristic signs Such a murmur is not uncommon in the healthy young and it may appear in middle age I have followed cases showing this murmur for twenty to thirty years and in none have there been any serious consequences caused by the condition giving rise to the murmur How it is produced I do not know

After repeated attacks the patient s life becomes one of great limitation The future depends often on the rapidity of the advance of the sclerotic process of the valves and the heart muscle If the rate of advance be slow and the heart muscle capable of responding to treatment the patient may go on for many years with a crippled existence Sometimes at the post mortem examination we find in the young about twenty years of age the orifice narrowed to a mere slit In others we find the mitral orifice not much contracted but the heart wall greatly dilated and evidence of fibrosis of the muscle Hence it will be seen that the progress of these cases is largely dependent on the rate of change in the muscle as well as in the valve The final issue is usually by great extension of the dropsy and exhaustion

The damage done by the rheumatic fever may effect other structures than the valves and as a result we get some curious effects upon the rate and rhythm of the heart The most common is an invasion of the auriculo ventricular bundle giving rise to a slight degree of heart block similar to that shown in Fig 1 This may appear during the causative attack of rheumatic fever or it may only show itself in after years Usually there is no sign of its presence unless a graphic record of the jugular pulse or an electrocardiogram is taken Occasionally it can be recognized by the dropping out of a ventricular beat as in Fig 1 when the stimulus from the auricle fails to pass to the ventricle This is apt to occur during the administration of digitalis

An interesting evidence of heart block is found in the mid diastolic murmur When mitral stenosis is present and there is a mild degree of heart block there is a delay after the murmur due to the auricular systole before the first sound occurs If a graphic record of the jugular pulse be taken there will be found a wave due to the auricular systole and this exactly synchronizes with the time of the murmur so that a mid diastolic murmur is an evidence not only of mitral stenosis but of partial heart block evidence that is of a damaged mitral valve and a damaged heart muscle

In advanced cases when there has been myocardial damage a curious variety of phenomena may appear especially under the influence of digitalis Thus attacks of paroxysmal tachycardia due to auricular flutter and auricular fibrillation may occur spontaneously I have seen in a few cases the latter condition arising from the administration of digitalis In one case with a mid diastolic murmur digitalis had a very peculiar effect causing a standstill of the whole heart and when the heart started the ventricle began before the auricle (Fig 10)

At various stages patients may be seized with great bleeding from the lungs Here doubtless the cause is engorgement of the pulmonary circulation and rupture of a blood vessel As a rule this is a grave sign the patient dying sometimes shortly after an attack, although in auricular

fibrillation the patient may make a good recovery especially if the heart is susceptible to digitalis In rare cases the curious and usually fatal condition suffocative edema of the lungs may unexpectedly occur

Vegetations may grow on the mitral valves with no certain sign of their presence until a small portion is detached and impacted in some vessel gives rise to a hemiplegic attack or an attack of aphasia Usually recovery takes place speedily and may be permanent but cases have been recorded in which the aphasia or hemiplegia has remained complete for many years Clotting may occur in the auricular appendage during auricular fibrillation and be a source of embolic infarct

Attacks of angina pectoris although very rare may occur in mitral stenosis In the few cases I have observed they were all secondary to

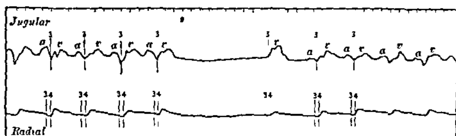


FIG 10—Simultaneous tracings of the pulsation in the jugular at the same time as the radial showing the temporary arrest of the whole heart from digitalis The first beat after the long pause is an escaped ventricular beat there being no auricular beat preceding it The waves *a* are due to the auricle and the waves *r* are due to the ventricle

some excessive exertion and the patients had only one or two attacks remaining perfectly free from them for years afterwards

AORTIC STENOSIS

Aortic stenosis is often associated with aortic regurgitation and the symptoms of the latter usually dominate the situation When there is little or *no regurgitation* the murmur of aortic stenosis may only be detected in the routine examination of the patient

Aortic stenosis which embarrasses the left ventricle is by itself a rare condition I have only seen it in a few elderly people in whom there was a syphilitic history A systolic murmur at the base of the heart should never be taken as indication of aortic stenosis without other characteristic signs Such a murmur is not uncommon in the healthy young and it may appear in middle age I have followed cases showing this murmur for twenty to thirty years and in none have there been any serious consequences caused by the condition giving rise to the murmur How it is produced I do not know

The sign characteristic of aortic stenosis is a murmur systolic in time heard loudest over the second right costal cartilage propagated into the carotids and accompanied by a thrill perceptible over the upper part of the chest wall The heart s rate is often slow between fifty and sixty beats per minute The radial pulse is sometimes very characteristic It impinges against the finger in a slow leisurely fashion and a sphygmographic tracing may show a slanting up stroke with a slight interruption near the summit (anacrotic pulse) or even a double wave at the top (pulsus bisferiens)

Besides these signs there is little that is characteristic in aortic stenosis There may be symptoms of angina pectoris but these are due to associated changes in the heart muscle and other evidences of heart failure can be referred to the same cause

Aortic Regurgitation

The aortic valves being contracted are no longer able to support efficiently the column of arterial blood during the diastole but permit a backward flow into the heart and as a result we find certain alterations in the character of the second sound and of the arterial pulse The closure of the valves no longer gives to the second sound the characteristic snap but the sound ends in a murmur sometimes long drawn out sometimes so brief as to be scarcely perceptible as if the second sound terminated not abruptly but with a faint sigh The diastolic murmur is usually propagated down the sternum but sometimes it is heard loudest at the apex It has been suggested that this variation in the propagation of the murmur depends on the direction given to the backward flow by the position of the retracted cusp This seems plausible but I have not been able to verify it and the explanation is ignored in recent textbooks

The regurgitant murmur is usually associated with the murmur of aortic stenosis and we get the characteristic double aortic murmur (bellows murmur) There is frequently dilatation of the smaller arteries and this combined with the effect of the regurgitation on the arterial pulse causes the artery to become emptier than usual towards the end of diastole This means a fall of pressure and in order to maintain a normal mean pressure the heart increases the force of its contractions raising the pressure during systole so that there is a great increase in the systolic pressure and a great fall during diastole thus giving rise to the characteristic collapsing pulse (Corrigan s pulse the water hammer pulse) The collapsing character of the radial pulse may be intensified by raising the arm above the head At times the arterial pulse is conveyed through the capillaries into the veins and is visible on the back of the hand If the forehead be rubbed so as to produce redness the flush is seen to wax and wane with each beat of the

heart (capillary pulsation) and these same phenomena appear in the finger nails.

The double aortic murmur may be present without any history of a heart affection. In many cases there may be little or no dilatation and the individual may be able to indulge in games and in occupations requiring considerable exertion with no discomfort. In such cases it may safely be assumed that the damage to the valves has been slight and that the heart muscle has escaped serious injury.

In other cases the heart is greatly enlarged and the apex beat is diffuse and forcible. The systole and diastole of the heart may cause movements of the liver that simulate pulsation of that organ, but analysis of its graphic records shows it to be merely the dragging up and pushing down of the liver by the changes in the size of the heart. Even under these circumstances the individual may for years pursue an active life, but he is always liable to attacks of heart failure. The condition is often associated with diseases of the mitral valves, and this is one of the factors participating in the production of the heart failure that finally terminates these cases.

The most frequent sufferers from heart failure due to aortic valvular disease are in middle age. In them the sclerotic process has been gradually advancing and the early symptoms of exhausted reserve force have been neglected until symptoms of distress command attention. There may have been a history of rheumatism, of excessive drinking, or hard bodily exertion, of syphilis, but on the other hand no definite causal condition may be discovered. The facial aspect is frequently of a pale gray (earthy countenance), though in others in whom there are other complications it may be full blooded and ruddy. *The complaints are varied. Shortness of breath* on exertion, violent throbbing in the neck, attacks of pain over the chest on exertion are amongst the most common symptoms of which the patient complains in the early stages of heart failure. For a varying period under suitable treatment a certain store of reserve force is gained and he may go on for months or years, sometimes in fair comfort, but his existence is usually more or less crippled after the appearance of signs of functional inefficiency.

A feature strikingly characteristic of aortic regurgitation is the susceptibility to nerve stimulation. The heart and blood vessels are readily stimulated, the former to rapid action, the latter to variations in the caliber of the vessels. The recognition of this peculiarity is of importance, for I have repeatedly seen individuals in whom the heart became rapid in action and with consequent exhaustion when they were first informed they had an affection of the heart. Moreover these cases are very susceptible to a mental stimulus which may increase the heart rate and also raise the blood pressure and induce attacks of angina pectoris. The difference of

the blood pressure in the arteries of the arm and leg has been commented on and also the susceptibility to attacks of pain

The end of these patients is very varied Many aortic cases suffer from extreme exhaustion and may show no objective signs of heart failure such as dropsy Where there is dilatation and dropsy it is generally because there is present some disease of the muscle wall as shown by the presence of auricular fibrillation Some of the most intractable cases of auricular fibrillation are those where there is also aortic regurgitation so that I look upon the appearance of auricular fibrillation in aortic cases as a somewhat grave event more so than when it occurs with mitral stenosis Those who suffer from angina pectoris may die suddenly I have seen a few cases die during a sudden attack of dyspnea of the greatest severity

Prognosis

In estimating the value of any abnormal sign or in determining the condition of the heart the most reliable guide is the manner in which the heart responds to exertion This again is but an attempt to estimate the amount of reserve force If the individual can with comfort make such exertion as we would expect at his time of life then the abnormality may with certainty be assumed to be of little real significance

If there be a complete breakdown the decision should not be made until time has shown to what extent recovery takes place The amount of recovery enables us to judge the condition of the muscle of the heart for it is on its capability to renew its reserve force that the future of the patient depends An axiom applicable to a great many cases is that patients usually recover from their first attack of heart failure however extreme it may be The reason for this is that the patient has persistently been giving a crippled heart more work to do than it was fit for so that a period of rest is sufficient to restore a measure of strength to the exhausted muscle

Even cases that never show a complete restoration of function and in which attacks of extreme failure are frequent may go on for many years and the individuals lead sometimes fairly useful lives though in time the progressive changes become so great or the muscle so exhausted that the possibility of even temporary recovery is precluded

In individuals in whom there is a distinct limitation of the field of cardiac response a close scrutiny should be made into the cause It should be borne in mind that if a heart is not properly exercised its field of response becomes more and more restricted Thus a man who for a long time leads a sedentary life is often startled by the fact that he is rendered extremely breathless by undertaking some exertion that he was wont to make with ease a few years previously But with moderate training there is soon

restored sufficient reserve force to enable him to perform his task without distress Therefore in all cases even when there is an abnormal symptom as a murmur or an irregularity the nature of the exhaustion should be discovered It must not be forgotten also that the supposed abnormality may have nothing to do with the symptoms of exhaustion This is particularly the case in the young in whom syncopal attacks are not infrequent I have repeatedly seen grave alarm aroused because a boy or girl has fainted and has had an irregular pulse when quiet in bed This irregularity has been of the youthful type and had no connection with the syncopal attacks and its presence in no sense added any gravity to the condition

While the lines on which prognosis is based can be fairly well recognized in regard to the more common affections of the heart we often meet with patients who show symptoms whose nature is too obscure for us to identify A prognosis in these cases is often required and difficult to give The plan I have adopted is to exclude the possibility of degenerated muscle by an examination of the condition of the heart muscle and particularly its efficiency as laid down under heart failure We should always consider how far the subjective complaints may be nervous in origin Having satisfied myself that the muscle is sound I give a favorable prognosis at the same time indicating the obscurity of the case I do this because as a matter of experience I have found that these exceptional cases particularly in young adults always tend to recovery to a greater or less degree This unfortunately is not the usual plan for some signs are too often taken to be more serious the more obscure they are In many cases the physician must be prepared to back up his opinion by taking a certain amount of responsibility For instance I have on several occasions seen patients kept in bed and put through elaborate forms of treatment after an illness as influenza or an attack of angina pectoris The patients have complained of obscure signs to them alarming and a certain amount of abnormality has been present as a frequent pulse or extrasystoles Having satisfied myself that there was no serious mischief I have had no hesitation in making the patients get up and resume their ordinary life even when the medical attendant has shrunk from the responsibility I have never yet had cause to regret such a procedure and it is better to run a little risk in a rare case than to have a patient drifting to invalidism because of our ignorance and fear of responsibility

Prognosis in Valvular Affections —Let it always be remembered that sound and healthy hearts may show a murmur and that it is necessary therefore to seek for other evidences on which to base a prognosis The heart failure which may be present depends upon so many and so varied conditions as the extent of the valvular lesion its progressive nature depending on the cicatrizing process affecting the valves the coincident

changes in the muscle and in the auriculo ventricular bundle the condition of life of the individual that no rule applicable to all cases can be made If however an attempt be made to appreciate the value of the symptoms present on the lines I have laid down an approach to a true prognosis may be made in each case There is just one point I again wish to insist upon let no murmur be the ground for forming an unfavorable prognosis In this respect the presence of a murmur has so oppressed the profession that a vast amount of positive harm is continually being done to patients by an imperfect understanding of the prognostic significance of this sign The field of cardiac response is the only true and safe guide in these cases If for the time being this is limited judgment should be suspended until an opportunity has been obtained for ascertaining to what extent the heart muscle can regain a store of reserve force

Treatment of Heart Disease

The highest aim of the medical profession is to prevent and cure disease Unfortunately this is rarely possible and the chief occupation of the doctor is the relief of suffering and the attempt to modify the course of disease As has been pointed out diseases of the heart are already present in the vast majority of cases when the doctor sees the patient so that the most he can do is to make the best of a damaged heart Fortunately in the majority of cases if the doctor understands the source of danger and recognizes the signs which indicate danger he can do a great deal for his patient But this question of understanding the significance of signs is a matter of the greatest importance The knowledge that death comes frequently through heart affections oppresses patients and doctor The former being told his heart is affected becomes willing to submit to treatment and restrictions that hold out the hope of recovery The doctor having no clear idea of the significance of signs employs too often all sorts of methods in the hope that he may by good fortune help his patient In the past the absence of a clear idea of the source of danger led to the assumption that practically every abnormal sign or what was taken for an abnormal sign was a call for treatment The statement that signs such as murmurs or irregularities were frequently of no serious significance were indeed physiological manifestations indicative neither of disease nor impairment is received today by many doctors as incredible The fact that a great many people who show these signs are in perfect health but have been subjected to treatment and have afterwards led vigorous lives has been taken as an evidence not of the innocence of the symptoms but of the efficiency of the treatment For this reason there is now recommended for treatment of affections of the heart such a great number of methods drugs baths exercises that the

utmost confusion surrounds a matter which can be rendered simple and easy of comprehension when the fundamental principles of therapy are understood

To appreciate these principles it is necessary to grasp wherein the danger lies The danger in every case of heart affection is that the heart may fail to maintain an efficient circulation I have already dealt fully with this matter and have shown that the maintenance of an efficient circulation depends on the integrity of the heart muscle An inquiry into the signs which indicate heart failure showed that in the first instance the failing heart could be recognized by distress being provoked when the individual made some effort which he was wont to perform in comfort The later stages of heart failure are exhibited by such signs as dropsy enlarged liver and orthopnea That is to say the signs of heart failure are shown by signs of a deficient circulation in other organs This way of looking at the matter enables a classification of symptoms to be made which directs attention to their significance inasmuch as it shows that the physical signs revealed by the examination of the heart itself by the unaided senses or by mechanical devices give no clue to the functional efficiency of the heart The great importance of this classification will be seen when it is reflected that hitherto the discovery of a physical sign has been looked upon as an indication for treatment

If then we bear in mind the view that heart failure begins by an exhaustion of reserve force, and is perceived only when exertion is made to the full amount of which the heart is capable the first duty in treatment is to ascertain what circumstances have induced the heart failure To this end an inquiry is made into the patient's condition to find out when he first became conscious of the limitations of his cardiac field to response Then a searching examination is made into the circumstances preceding that period as to the question of overwork worry sleeplessness or infection The inquiry next proceeds to the examination of the circulatory system and any defect there must be considered from the point of view whether its presence embarrasses the heart in its work and whether the failure has been due to a gradual weakening of the heart from this cause If the physician is careful to bear in mind that an abnormal sign is not necessarily an evidence in itself of disease and that it is not the sign which has to be treated but that the essential aim in the treatment of the heart failure is the restoration of the reserve force of the heart muscle then he will have a sure guide in applying treatment to the diverse conditions even when the symptoms are not fully understood Before proceeding to treat the patient we try to appreciate the value of his symptoms subjective as well as objective When we do find some abnormality on physical examination its bearing upon the subjective sensations has to be considered on the lines already laid down

and all attendant circumstances that may have contributed to the heart failure must be taken into consideration When we detect some actual cardiac defect and we do recognize that the heart failure is undoubtedly brought about by its presence then provided that we cannot remove the actual lesion the object of treatment is to restore the exhausted muscle and place the patient in such a position that he can lead a life useful and free from discomfort though hampered by an obstacle to the heart s full efficiency We should keep steadily before our view the fact that the heart is impaired and it is vain to attempt to restore the irremediable

This suggestion may seem so self evident as scarcely to need remarking still less to be emphasized but from practical observation I feel the necessity of insisting upon it for patients with an incurable cardiac defect are continually being subjected to treatment whenever they consult a physician and they may be found going to health resorts year after year under the impression that in some way or other the defect needs treatment If the patient had an ankylosed joint or a wooden leg it would be recognized that baths or drugs can do little for him, but the thickened edges of a mitral valve are supposed in some way to need constant treatment The object of treatment should not be to try to remove what cannot be cured but to make the best of what power the heart still possesses In the nature of things it may be that only a partial restoration of the heart can be looked for and when we recognize that the fullest amount of recovery has been gained judicious advice as to the future life of the patient may cause him to lead a life at a lower level it is true but still useful and interesting and his years may be prolonged to the allotted span Many individuals with a reserve force limited on account of inherent defects in the heart may never suffer from heart failure of any serious moment and where the lesion is not a progressive one they may suffer little inconvenience provided that their limitations be appreciated by themselves and their medical advisers It is in these cases that the advice of a wise physician is of great service The knowledge of how much an individual may do the permission to do as much as his reserve force will allow him without inducing exhaustion can only be acquired by the full and careful consideration of all the individual symptoms Much inconvenience may be caused to the patient by taking too grave a view of his cardiac defect and so limiting him far too strictly and hampering him in his life work and oppressing him needlessly with the supposed gravity of his condition On the other hand the pursuits of a man whose heart is embarrassed by a grave defect may imperceptibly call too frequently on the full extent of the reserve force of the heart and the period of rest being insufficient exhaustion of the reserve force gradually proceeds until heart failure of a more or less serious degree is induced The work of man has attained a rough and ready standard in most trades and

professions and the amount is fairly commensurate with the reserve force of the average healthy man The man with a cardiac defect is handicapped in the race and if the handicap is too heavy his endeavor to keep his place is made at the expense of his heart s strength The inevitable result is exhaustion of the reserve force which advances slowly but surely

I put the matter in this way and dwell upon it with some insistence because if the physician guides the sufferer in his work he may give life and hope to many a stricken fellow Thus in the early years after some cardiac lesion following rheumatic fever or other infective complaint the choice of a profession which will never entail severe bodily exertion may enable the lamed individual to live a useful and contented life In more advanced years the recognition of early stages of some progressive lesion as cardio sclerosis may enable the physician to advise the patient to avoid certain deleterious influences in his work or mode of life measures which may diminish the progressive exhaustion of his reserve force and enable him to pursue a useful and comfortable existence for an indefinite number of years The same applies in the many other ways in which a heart trouble may mar a patient s life as for instance the question of pregnancy and its relation to heart trouble a subject indeed of the first importance but unfortunately too little considered

It may reasonably be asked what are the indications which should guide the physician in advising a restricted life? No answer can be given of definiteness sufficient to be applicable to every case It is in this respect that a wise judgment needs to be exercised Many symptoms are so obscure in their origin and there is such a tendency in the human mind to see evil in what is not understood that a very urgent caution has to be given not to attach too grave a significance to any sign or symptom The more common forms of these have been dealt with in their appropriate chapters here I would lay down the general proposition *let no single abnormal sign of itself be the reason for giving a prognosis or for subjecting the patient to treatment* A careful search should be made for accompanying symptoms and a careful inquiry into the condition of the reserve force and the reason for any exhaustion and on the result of such an examination the final decision should be based

When the heart lesion is not progressive the best line of advice is that the patient should follow his trade or profession so long as it does not involve overexhaustion of the reserve force and indulge in such exercise as he can in comfort avoiding all forms of effort that induce distress When effort that may involve strain has to be undertaken a period of rest should follow sufficient to permit full recuperation By this line of conduct the heart itself will benefit by the judicious exercise of its functions and the patient will be freed from the restrictions of an invalid life

and all attendant circumstances that may have contributed to the heart failure must be taken into consideration When we detect some actual cardiac defect and we do recognize that the heart failure is undoubtedly brought about by its presence then provided that we cannot remove the actual lesion the object of treatment is to restore the exhausted muscle and place the patient in such a position that he can lead a life useful and free from discomfort though hampered by an obstacle to the heart s full efficiency We should keep steadily before our view the fact that the heart is impaired and it is vain to attempt to restore the irremediable

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excitement Bodily effort is not the only cause of exhaustion in many people *an irritable mechanism playing upon the heart induces a reaction that* is peculiarly exhausting In many sensitive nervous people the readiness with which *the heart responds to stimulation constitutes* the real source of the trouble and in time leads to very marked exhaustion especially if the heart is affected by some organic lesion In some cases more good can be done by treating the nervous element in the case by finding out and removing the cause of the excitability or by removing the patient to more congenial surroundings as to an environment which will interest without exciting or by dulling the nervous system with such drugs as the bromides

Worry business or domestic plays an important part in depressing the heart s functions and when it is not possible to free the patient from such conditions altogether steps should be taken to mitigate them as far as possible Other forms of mental disquiet should also be inquired into and treated Sleeplessness disturbed sleep and unpleasant dreams do much to hinder a patient s recovery and aggravate the heart failure It may be said with truth that no heart can regain its full strength if sufficient sleep is not obtained The various remedies for obtaining sleep will be considered later

These suggestions have reference to rest as applicable to the milder forms of heart failure Rest is of far greater value in cases of extreme heart failure where the reserve force is practically exhausted and the rest force is being encroached upon that is to say *the exhaustion has become so great* that the symptoms do not abate when the patient is laid in bed While *this condition demands the exhibition of other remedies than that of rest* yet rest itself is of the utmost value In these extreme cases it is not always *easy to find the position the body should occupy that is the most beneficial* As a rule the patient s sensations are a very good guide It may be that *lying in bed causes such distress that the patient is not at ease unless he* assumes some position which he finds removes the discomfort such as sitting *in a chair leaning forward* on a support Such *individuals should be permitted* to assume the position in which they find the most comfort or at least *the least discomfort* as it favors the circulation *in regions which induce* the distress as in the lungs or brain though it may militate against *the circulation in other regions* as in the legs When dropsy *tends to increase* in such cases careful change in position raising the legs as high as *possible deft bandaging and massage* may do much *to diminish the swelling* other treatment being at the same time directed to the dropsy and heart condition When the failure is not so extreme and particularly *if there is* dropsy complete rest in bed is of the greatest service and many cases recover without other means *If necessary* the shoulders may be raised by pillows or a bed rest to such a height as may prevent attacks of dyspnea

When the heart failure persists in spite of restriction of effort and the removal of injurious influences further measures must be adopted The periods of rest must be increased and remedies that may help the heart administered The administration of drugs of the digitalis group may be called for in certain states when the rate of the heart is increased and exhaustion is due to this cause, as auricular fibrillation In acute cases with fever digitalis is not indicated for treatment should be directed to the cause of the fever When there is evidence of a progressive lesion of the heart the amount of effort must be reduced to the lowest possible When the heart failure is extreme and the rest force is being exhausted as shown by the persistence of objective symptoms of heart failure such as dropsy difficulty in breathing etc, then there are indicated absolute rest the pushing of such drugs as digitalis until their physiological effect is produced and the treatment of special symptoms by appropriate remedies Sleep must be obtained if necessary by opium or chloral, if the milder hypnotics fail The food must be carefully regulated the movements of the bowels must be attended to and aperients or enemata given if necessary *If there* is much dropsy and congestion of the liver, a smart mercurial purge may be of use If however the movement of the bowels induces extreme exhaustion they had better be left alone for the time being

Rest

It may seem unnecessary to dwell upon such a well recognized agent in cardiac treatment as rest were it not for the fact that its effects are seldom fully appreciated In a great many systems of treatment rest is only one of the factors employed and the resultant benefit is rarely attributed to the rest but to some other agent that has been employed at the same time such as baths massage drugs movements change of residence If the value of simple rest of body and mind were sufficiently appreciated we should hear less of the vaunted cures by special methods

When a heart is exercised to the exhaustion of its reserve force it is absolutely necessary that a period of rest should follow of sufficient length to permit the restoration of this reserve force If the rest is not sufficient the exhaustion gradually becomes more readily induced and the signs of heart failure become more obtrusive Recognizing thus the potency of rest in maintaining the working power of the heart we can readily appreciate its beneficial effect in treating heart failure We have therefore to consider how best the necessary rest can be obtained In many cases by diminishing the amount of the day s work a longer period of rest may be obtained which is sufficient to restore the exhausted heart Other means for obtaining rest for the heart can be employed in protecting the heart from undue

of time appeals to him As one who has watched many of these patient over periods of many years I have seen no convincing evidence that the various abstemious dietaries that I have tried and seen others try arrest the progress of senility With advance of years the appetite diminishes as a rule and this is good as the process of assimilation also becomes restricted While moderation in all things is good it is difficult to tell what are its limits

Exercise

Every organ of the body is benefited by the judicious exercise of its functions When the patient is fit to go about he should be encouraged to take exercise in the fresh air The amount of exercise he may take will depend upon his strength and this can be gauged by his sensations So long as a man who is taking exercise remains free from distress or discomfort then the exercise is doing him good The principles underlying this statement will be realized if the nature of heart failure is understood We get indeed in this statement a guide which will serve us in all cases and we may lay it down that the patient should diminish or cease his efforts on the first appearance of a distressful sensation

It is far better that the patient should take his exercise in the fresh air in some form congenial to his temperament and suitable to his strength than that he should take it by making systematized movements or undergoing what are called graduated exercises To every case of heart affection there is a mental side mechanical exercises tend to remind the patient that he is an invalid whereas a game or an exercise in the fresh air with an object beyond the consideration of health has a beneficial mental effect In stating that the patient should take that amount of exercise which gives pleasure and does not give rise to sensations of distress or discomfort I am enunciating a principle of the highest importance If it is recognized by what means the heart failure has been induced and the nature of the symptoms which it provokes the significance of this principle will be grasped for exhaustion of the heart muscle shows itself in the first instance by producing sensations of distress on exertion

Moreover as all organs benefit by the judicious exercise of their functions so likewise the heart is kept in good condition by the exercise of its functions so long as the exercise does not produce exhaustion This truth has been clearly perceived and a great many forms of exercise have been evolved On behalf of some of these the resistance exercises of Schott for example fantastic claims have been made Other methods such as the graduated exercises of Oertel may have been found useful but these exercises are not based on a proper recognition of the object aimed at The object is the strengthening of the heart muscle by summarily laying down

coming on during sleep In all cases mild or severe every source of discomfort from other parts of the body should be attended to such as an irritating skin affection piles or frequent micturition

FOOD

In cases of extreme heart failure with dropsy the food should be limited in quantity as a rule small quantities of milk given at frequent intervals in some cases not more than one pint a day The patient should be encouraged to take a small portion of biscuit, or a dainty sandwich with fresh potted meat chewed very thoroughly The mouthfuls should be small especially when there is labored breathing In febrile cases or when the mouth tends to become dirty it should be washed and sponged out and immediately afterwards a small piece of solid food should be given to chew

In less severe cases the food should be more varied but it should never be forced on the patient The quantity he can chew is often a very good guide because if he cannot be tempted to chew very much it is manifest that his digestive organs are at fault and it is a very bad practice in such cases to pour in beef tea and other easily ingested foods The guiding principle should be food tempting needing mastication with little fluid and that chiefly milk given in small quantities and at fairly frequent intervals these to depend on the quantity he is able to take The kind of food should be that which the patient likes so long as it does not disagree with him Food which causes discomfort or distaste should not be forced The doctor must be on his guard not to prescribe a dietary suitable to himself but must bear in mind that what disagrees with him may agree with the patient In selecting a dietary the resources of an intelligent housewife will often be found to be of much service

Individuals with heart trouble but able to get about should lead a life of abstemiousness avoiding all excesses The meals should be small in quantity and of such frequency that all faintness is avoided It often happens that they become faint in the night or early in the morning as they have not broken their fast since the evening meal A dry biscuit and a small cup of milk at bedtime or in the early morning will often prevent the occurrence of disagreeable sensations

A class of people for whom many dietaries have been evolved are those who with advancing years show some signs of wear and tear It may be that in their vigorous manhood they enjoyed and gratified excellent appetites but as the years begin to tell the pleasures of the table no longer appeal to them Signs of the heart failing may appear and the individual begins to take thought and seeks advice Such a one readily becomes the victim of a dietetic craze A course of life that seems to put back the hand

of the heart and blood vessels but it requires an intelligent appreciation of their effect and of the condition of the heart before they can be used as remedies The same appreciation is required in the use of drugs

It has long been known that exhaustion and rapid heart action are frequently associated with heart failure and the employment of drugs that reduce the rate of the heart has often been followed by a great improvement in the patient s condition Drugs which have this effect belong to a definite group of which digitalis and strophanthus are the best known and the most effective They seem however to have a very restricted action chiefly limited to the slowing of the heart s rate in certain abnormal rhythms of the heart This is probably due to their action on some part of the regulating mechanism of the heart s rate chiefly if not entirely through the vagus Whether these drugs have any action beyond slowing is doubtful except it may be in their effect upon that somewhat mysterious function of the heart muscle tone

Digitalis—In an inquiry I have conducted for many years on the action of this drug in every instance where I got a good result from its action on the heart it was accompanied by a diminution of the heart s rate If we remember that heart failure comes through exhaustion of the heart muscle and that exhaustion may arise from a persistent increase in the rate we may have here the reason for the remarkable efficacy of the digitalis group of remedies in certain diseases Apart from these cases in which improvement occurred with slowing of the rate the only other condition I have found benefited by digitalis was in dropsy when the digitalis acted as a diuretic I do not think that its action as a diuretic is dependent on its action on the heart for I have found it effective in this way before it showed any effect upon the heart and in heart block with the rate persistently at thirty beats per minute the diuretic effect has speedily removed the dropsy with a marked improvement in the patient s condition with no change in the heart s rate

Hitherto digitalis has been prescribed in a rule-of-thumb fashion Whenever a cardiac abnormality was detected it has been taken as an indication for the use of digitalis As it was given in every case with no accurate observation as to the kind of case in which benefit accrued from its use its administration was surrounded by so much confusion that its uselessness on the one hand and its usefulness on the other were not clearly recognized so much so indeed that its full beneficial effect in the cases where it was of use was never fully obtained

The best effect of digitalis is seen in cases of heart failure with dilatation of the heart and dropsy Eighty or ninety per cent of such cases suffer from auricular fibrillation and the heart failure is often induced by the very rapid rate that occurs with the onset of auricular fibrillation The

that so many yards should be walked one day and so many another day the physician shows that he has failed to take into account the peculiar nature of the heart functions. Thus the power of response of the heart to effort varies greatly in the same individual from time to time: one day a patient with an impaired heart can undertake a good deal of effort with comfort, whereas on other days the same amount of effort causes him distress. This is due to the fact that the heart may be embarrassed by a variety of conditions, such as gastric and intestinal disturbances, want of sleep, and the state of the weather. The patient's sensations are therefore a valuable guide, and indicate the amount of effort which can be undertaken by him with safety in all circumstances.

Baths

The immersion of the body in water at different temperatures has a great effect upon the peripheral circulation and also modifies the rate of the heart. When the temperature of the bath is above that of the body the peripheral vessels dilate and the heart's rate increases; when it is below that of the body the peripheral vessels contract and the heart's rate diminishes. It is doubtful whether these varied reactions have any permanent effect on the heart. That a warm bath may afford temporary relief in special circumstances may be quite true. Great therapeutic efficacy is claimed for certain waters, but it is very doubtful if the ingredients in these waters have any effect upon the heart beyond their effect in stimulating the skin. My personal experience has been limited to observing the result in patients who have returned from the various spas, and I have seen nothing of their good effects to lead me to place hydrotherapy very high as a means of treating affections of the heart. The best results I have seen have been in patients who have bathed in the open sea. When I have had patients with heart trouble who were fond of sea bathing I have allowed them to indulge in it, warning them to be honest with themselves and refrain if it brought on any sense of discomfort. In many cases the result has been extremely satisfactory; the whole system of the patient has been braced up, and they have returned from the holiday greatly benefited.

Drugs

There are a number of drugs that have an effect upon some parts of the circulatory apparatus, and these are employed for remedial purposes in affections of the heart. There is an idea that because a drug or a method has some demonstrable effect on the circulatory system it is therefore of use in treatment. In baths and exercise we have means of modifying the action

of the heart and blood vessels but it requires an intelligent appreciation of their effect and of the condition of the heart before they can be used as remedies The same appreciation is required in the use of drugs

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response of the heart to digitalis in some of these cases is almost dramatic Patients may suffer from orthopnea Cheyne Stokes respiration extensive dropsy and a heart over 130 beats per minute small and irregular but as soon as a sufficiency of digitalis is given the rate falls to 60 or 70 the dropsy disappears the patient lies down and all signs of distress disappear It is because of such remarkable results that digitalis has obtained its great reputation If we scrutinize the published records of cases that have benefited by the drug we find that the great majority of these results occur in one condition auricular fibrillation or its allied condition auricular flutter I have repeatedly given digitalis to cases of mitral stenosis with the normal rhythm and little effect was produced in the rate of the heart but as soon as auricular fibrillation occurred then the heart became very susceptible to its action It is well to keep this in mind because it leads one to inquire in every case of rapid heart into the nature of the stimulation which excites the heart to this rapid rate When the rate is due to toxic influences as the infections or exophthalmic goiter we never get this beneficial effect of digitalis Indeed my experience has been that with the normal rhythm only occasionally does the digitalis slow the heart and that to a very slight degree Dr George Sutherland tells me he has seen distinct slowing of the rate in young people with some rheumatic affection of the heart in which the heart s rate was greatly increased but I have not met with such cases

To adopt a rational treatment in cases of rapid heart it is necessary to find out the nature of the exciting stimulus and direct attention to that and not unintelligently to prescribe digitalis because it slows the heart in certain peculiar states The belief in its power of slowing the heart in all cases is so prevalent that a rapid heart, whatever the cause is *deemed to* require digitalis At one time a lively discussion took place in the medical journals as to the propriety of giving digitalis in aortic regurgitation It was held that the drug would be dangerous inasmuch as by slowing the heart it would prolong the diastole of the ventricle and thus increase the evil effects of the regurgitant stream of blood None seemed to be aware that digitalis does not slow the heart in aortic regurgitation at all events I have repeatedly pushed the drug till I obtained evidence of its physiological effect by vomiting with no slowing of the rate

Digitalis is often prescribed in angina pectoris and mild degrees of heart failure as in the early stages of mitral stenosis and success has been claimed for its use I must confess I have never seen any good effect in such case One usually employs the more potent treatment rest in such cases and the credit for the good that has been done is given to the drug Moreover the quantity of drug usually prescribed is so small that I doubt if it can have an effect of any kind

The form of preparation I have mostly used is the tincture which I have never yet found to fail me If it can be obtained of a guaranteed strength well and good but I soon find out for myself whether it is active I use the tincture because it is handiest and most reasonable in price a very important consideration to the general practitioner in practice amongst the working classes A more elegant preparation may be used and I have made a large number of observations with digitalin (Nativelle's Granules) One of these granules containing 1/240 grain (0 000_5 gm) I find has the same effect as about 15 minims (1 c c) of the tincture Many patients themselves buy digitalis leaves and make an infusion of variable strength but they get to know the physiological effect and treat them elves One man whom I had under observation for over thirteen years with auricular fibrillation used as a standard the degree of swelling of his legs his test being that when he could not comfortably lace up his boots it was a sign to take his home made infusion of digitalis

So far as I have seen there i no special virtue in the various extractives obtained from the digitalis leaf and I see no ground for according them priority over such a preparation as the tincture which includes all the different glucosides

In persistent dropsy due to heart failure greater benefit may be obtained when the digitalis is combined with mercury and squills (as for instance mercurial pill 2 grains or 0 12 gram powdered digitalis leaves ½ grain or 0 03 gram squills 1 grain or 0 06 gram) This combination is often useful when digitalis by itself is without effect One patient received much benefit from this preparation but she was so salivated by the mercury that the medicine could not be used for a sufficient length of time A number of other preparations of digitalis and of strophanthus were used without effect At last the patient took the pills with her food and for some reason she was not again salivated and was able to keep the dropsy in check

It is a common practice to seek a more speedy effect by hypodermic injections of digitalin and I have tested this method in numerous ca e but failed to get any effect from this method of administration It is often used when patients are dying from some grave affection as pneumonia as a last resort probably more for the purpo e of doing something than with expectations of great benefit I have never seen any good follow the ad in istration of digitalis in acute febrile states The factors exciting the heart such as high temperature toxins or the invasion of the heart by specific organisms exert an influence over the heart which the digitalis cannot over come I think it desirable to mention this as it is a waste of time and opportunity to apply remedies which are of no avail in urgent cases while by recognizing their uselessness we may search for more helpful measures

As a result of my experiences I push the digitalis until some physiological reaction occurs such as nausea diarrhea or slowing of the heart and then stop the drug for a few days I am confident that if an outlook is kept for such signs there need be no fear of poisoning or of any deleterious effect The dose therefore in any given case depends partly on the nature of the case In giving the tincture to an adult doses of fifteen to twenty minims (1 to 1 3 c c) thrice daily usually produce the effect in three to five days If the distress in breathing is great and the pulse rapid double the quantity may be safely administered and the physiological effect looked for in twenty four or forty eight hours

When a good effect is obtained from the use of digitalis the effect should be kept up This is done by stopping the drug when the rate has fallen below eighty or seventy and giving half doses as soon as the rate begins to increase By giving and withholding the drug the quantity necessary to keep the rate at a moderate level can be found The patient should also be instructed to correlate his sensations of relief with the fall of the rate so that he may acquire a knowledge of when it is necessary to take the drug If this is done intelligently many patients especially those suffering from auricular fibrillation may be able to lead a useful life for many years free from these attacks of extreme heart failure that are so apt to occur in this condition

Sometimes digitalis is spoken of as if it were a dangerous drug In inquiring into the source of danger I have found that the digitalis has been pushed after the signs of its reaction in the stomach or after great slowing of the pulse has occurred and patients have died suddenly I have been following the line indicated above for over thirty years and have not had a single death from its use

Strophanthus —Notwithstanding the assertion that the action of strophanthus differs from that of digitalis I could never in practice detect any difference Digitalis is perhaps more apt to produce intestinal disturbances as nausea than strophanthus and so occasionally when there is an objection to the use of digitalis by reason of the easy production of nausea strophanthus has been a useful substitute I have found strophanthus produces diarrhea very readily in a few cases On the whole when digitalis has failed to do good in my hands strophanthus and other drugs of the same class (squills cactus grandiflorus) have also failed

The tincture of strophanthus was found to be only half as effective as digitalis This conclusion was based upon the fact that double the quantity had to be given as a rule before a result was obtained The tincture of strophanthus should not be prescribed in a mixture with water as Cushny has shown that it deteriorates and after a few days becomes inert in such a mixture

Intravenous injections of strophanthin (1/100 of a grain or 0 5 milligram) act speedily but I do not advise their use in general practice if the doctor knows how to treat his patient intelligently by the use of digitalis Moreover the call for the use of strophanthin injections is a very infrequent one and when it does arise the same end which is served by intravenous injection can be accomplished in a few days by the oral administration of the drug Hypodermic injections of digitalin and strophanthin were found to be without any result the drug evidently not being absorbed

The Nitrites —The principal effect of the nitrites is a dilatation of the arterioles It is now accepted that the cause of the dilatation is the stimulation of the nerves and muscles of the vessel walls This effect is accompanied by an acceleration of the heart rate and a great fall in the arterial pressure When for any reason a sudden effect of this kind upon the heart is wanted the nitrites are the most potent drugs that can be employed A few drops (3 to 10 minims or 0 2 to 0 65 c c) of nitrite of amyl inhaled produce this effect in a few seconds The face becomes flushed and the patient is conscious of a throbbing in the head If the use of the drug be continued the patient becomes faint and giddy and is forced to lie down The drug should never be continued beyond this stage In a few minutes the effect passes off and the blood pressure which has undergone a sudden fall rises gradually and may even become higher than it was before the inhalation

Other nitrites such as nitroglycerin (dose 1/100 to 1/50 of a grain or 0 5 to 1 milligram in tablets or in alcoholic solution) erythrol tetranitrite (dose 1 grain in pills) sodium nitrite (1 to 2 grains or 0 065 to 0 13 gram in pills or solution) act in the same way as amyl nitrite but more slowly and the effect remains slightly longer

The best effect of the nitrites is obtained in cases requiring a rapid therapeutic action as in angina pectoris Some of the slower acting nitrites are recommended as reducers of a high blood pressure but I have had no satisfactory results from their use nor does it seem a reasonable procedure to use them when as so often happens the increased blood pressure may be due to some irritating substance circulating in the blood *e g* in kidney disease

Sedatives —Little benefit is likely to arise from treatment so long as a patient is worried or sleepless I have already referred to the importance of rest it is often necessary to seek the aid of drugs to obtain rest and sleep and freedom from worry and other excitations in these circumstances sedative drugs used with discrimination are of the greatest service

The bromides are the most useful drugs in this respect In all cases of mild degrees of heart failure where the patient is able to get about but where he is worried sleepless irritable or apprehensive or suffers from palpitation the bromides are extremely useful and of far more value than other

cardiac drugs I have for many years employed the bromide of ammonium for I find that the patients are not so depressed by its use as they are when taking the bromide of potassium The drug should be pushed until a slight lassitude is induced or even until the patient becomes torpid and this is true especially in severe cases of angina pectoris The doses employed are twenty grains or 1 3 grams two or three or four times a day according to the severity of the case

For sleeplessness the milder hypnotics the bromides phenacetin veronal and sulphonal may first be tried If these fail resort must be had to chloral or opium In great restlessness due to dyspnea Cheyne Stokes respiration or cardiac asthma one of these drugs should be carefully given until the desired effect is obtained 5 to 10 grains or 0 3 to 0 6 gram of chloral every two hours or ¼ grain or 15 milligram of morphia (⅛ grain or 7 5 milligrams hypodermically) repeated every two hours will often suffice When there is edema of the lungs or bronchitis the opiates should be avoided as they tend to check the free expulsion of the phlegm and danger may arise from this cause Neither chloral nor opium should be continued for more than a few days as the patients become sick mentally confused and very troublesome

Other Drugs—A great number of agents are used in cardiac therapy but it is doubtful if many of them have any real effect on the heart Some undoubtedly as for example alcohol and hot fluids can show evidence of a reaction the action of these in producing a dilatation of the arterioles can be employed with benefit when a rapid effect is desired *e g* in attacks of faintness or prostration It is scarcely necessary at this time of day to add a warning regarding the use of alcohol in milder forms of heart failure and particularly in those with a neurotic tendency The temporary benefit thus obtained may lead to a too frequent use of the drug The danger of habit being created cannot be overlooked

Other drugs such as caffein strychnin and oil of camphor act probably on the nervous system and by producing some exhilaration prove useful in cases where a temporary exhaustion causes distress But it cannot be too strongly insisted that though these remedies are often employed in cases of the most diverse kind for instance where there is a rapid heart in pneumonia and where there is a sluggish ventricle in heart block they are without any perceptible effect on the heart They should not be relied upon in cases of real heart exhaustion